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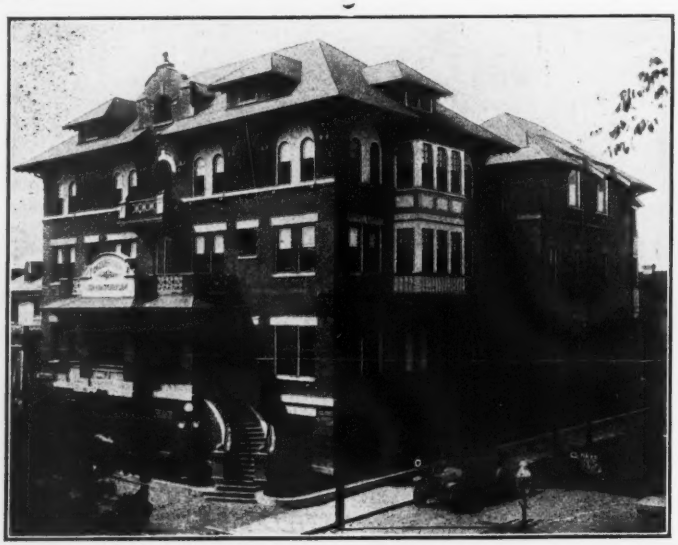

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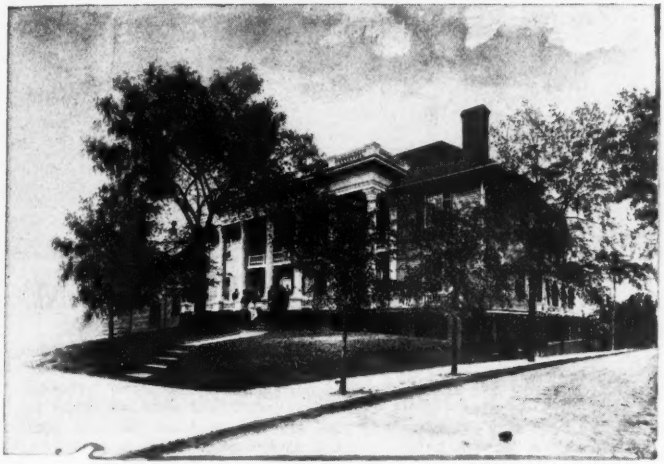

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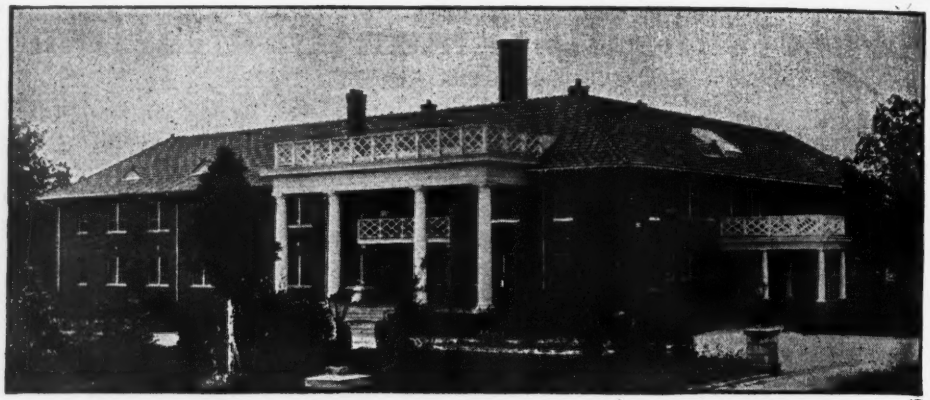

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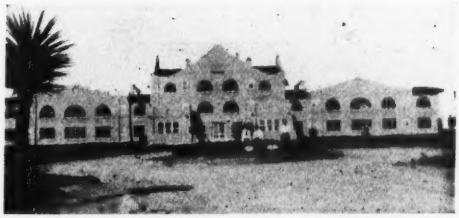

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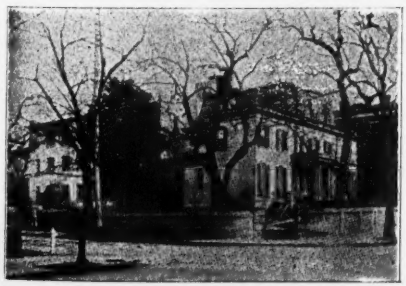

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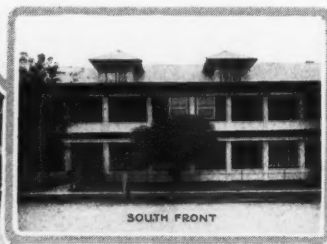

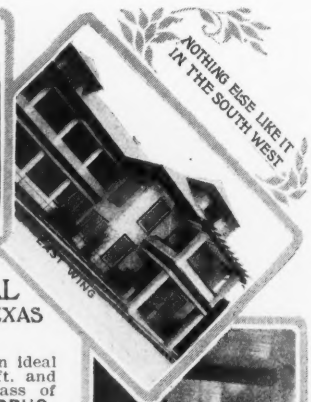

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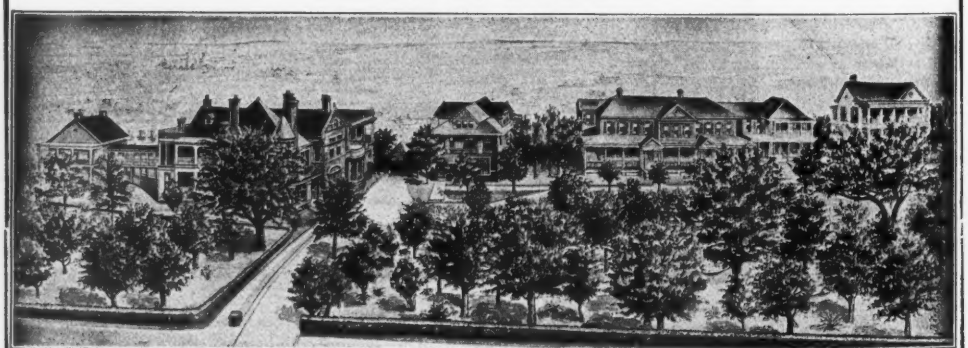

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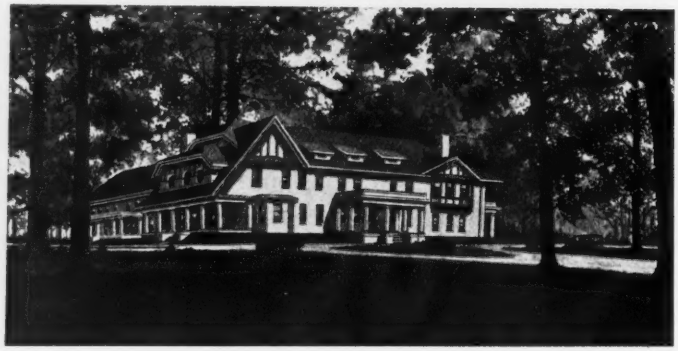

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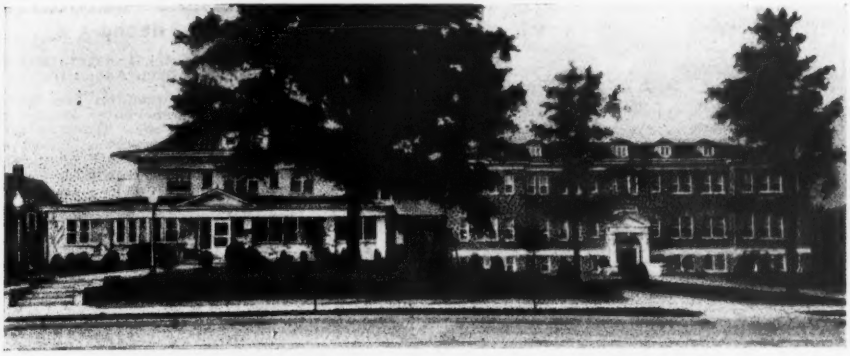

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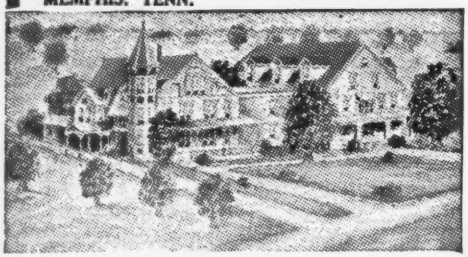

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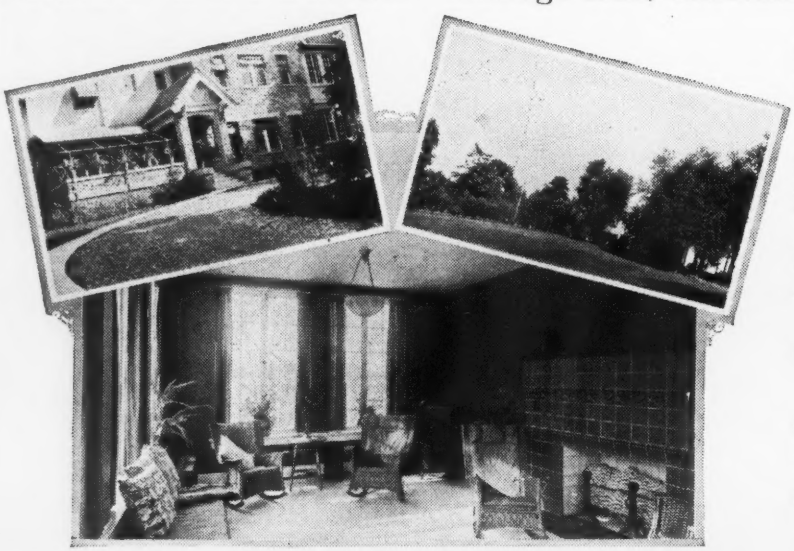

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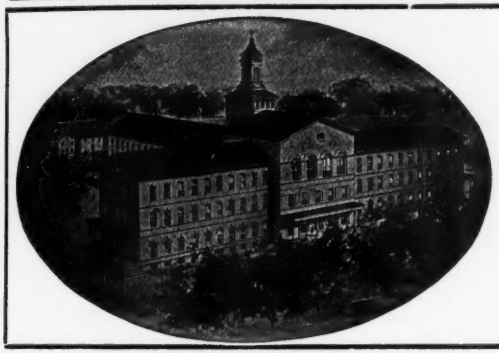

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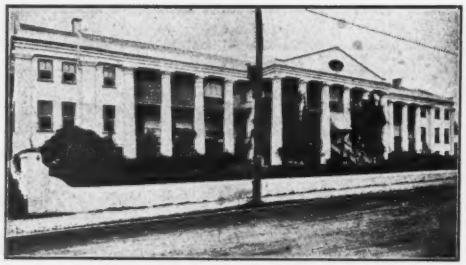

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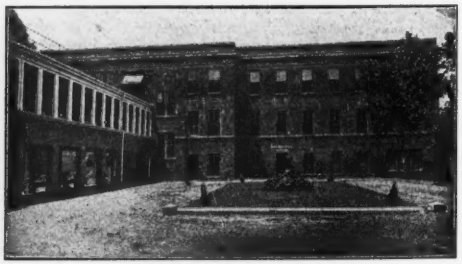

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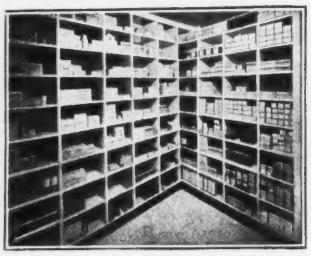

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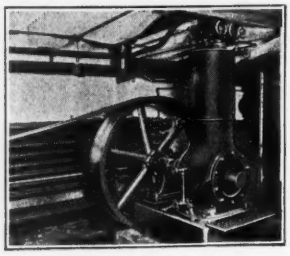

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SIR WILLIAM OSLER

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FOREWORD

OSLER AND THE SOUTH

By Lewellys F. Barker, M.D., LL.D.,
Professor of Clinical Medicine, Medical Department, Johns Hopkins University;
President of the Southern Medical Association,
Baltimore, Md.

Physicians in the South join gladly physicians throughout this country and the English-speaking world in celebrating this July the seventieth birthday of Sir William Osler.

That this great clinician on the 12th of the month attains the age of three score and ten, is still in good health and as active as ever in work that redounds to the credit of our profession, are sufficient causes for genuine rejoicing. They explain the eagerness shown by all who have known the man, and who are grateful for his influence, to mark this anniversary in some unusual way. Professor Osler's closer friends and pupils have contributed two volumes of original papers to be published in an "Anniversary Testimonial," and several of the weekly and other monthly medical journals are issuing Osler numbers in July, so widespread is the desire to join in honoring a man who not only stands for the best in modern medicine but who, on account of his character and personal qualities, has won the respect, the admiration and the affection of the whole medical profession. In this impulse to honor Dr. Osler, Southern physicians delight to share.

Indeed, there are special reasons why the South desires actively to participate on every occasion when opportunity arises to honor Osler, for, in the first place, since the major part of his professional life was spent in Maryland, building up a great medical clinic at the Johns Hopkins Hospital, the South regards him as peculiarly its own. In the second place, his patients were drawn largely from the South and the Southwest, and he had during his Johns Hopkins period a larger personal acquaintance with laymen and physicians in this great area than perhaps any other single medical man of the time. In the third place, many medical students in the South, as well as physicians seeking postgraduate instruction, flocked to him, and benefited by his teaching, and are now engaged in practice in the Southern states, carrying into effect the principles he believed in, and using the methods he employed. And, finally, it can be said with truth that Osler had a peculiar understanding of the minds of the people of the South, and that Southerners generally have felt that they could share with him a kind of intimacy that they could not experience with other leaders, even those whom they greatly respected and admired. It is but little wonder, then, that on July 12th of this year the thoughts of Southern doctors will turn toward the Regius Professor of Medicine at Oxford, and that their hearts will be filled with gratitude for this friend whom they revere.

On this anniversary, too, it would not be like the South to fail to include in its felicitations the one who, through work and leisure, and through joy and sorrow, has stood steadfastly by the side of him whom we honor. Those medical men of the South and their wives—now no small group—who in Baltimore, as in Oxford, have been privileged to enjoy the hospitality of the Oslers are the fortunate possessors of memories that they will always prize. The South likes to be known and deserves to be known for its hospitality. What greater praise in this regard could be given the Oslers than to admit that their genius for hospitality is worthy of the best traditions of the South? To these two friends, then, the South sends this month its greetings and its congratulations. For the man who has achieved and helped, for the woman who has adorned and blessed, and for the two together, who in the world war have made a greater sacrifice than life itself, we of the South cherish feelings that we can not adequately express. That they may both in their later lives have many years of health and happiness is the ardent wish of their host of friends in the South.

A TRIBUTE TO SIR WILLIAM OSLER

By Howard A. Kelly, M.D., LL.D.,
Professor of Gynecology, Medical Department, John Hopkins University,
Baltimore, Md.

The mere fact of having been permitted to live through the last forty years to witness the momentous changes and renovation of modern medicine is a sufficiently thrilling experience, but to have been like Sir William Osler, one of the most active participants in, and contributors to, those changees, is indeed a rare privilege; for with that rush which characterizes modern progress we have condensed within the short term of a few decades changes greater than those of all the preceding centuries.

In the midst of all these dramatic changes, Osler has lived as one who has had a large share in bringing them about. His biography is one of unusual interest because of the events through which he has passed, somewhat as a general leading a vast medical army, as well as because of the inspiration to be derived from his personal qualities.

The early Hopkins medical group was in many respects a combination such as hardly seems likely to repeat itself within the lifetime of the present generation. There was Welch, on the ground years before the rest of us, laying the foundation stones for the new medical school in pathology according to Gilman's ideas of the true basis of scientific medicine. There was Halsted, Welch's inseparable companion, also basing the scientific surgery of the future on pathology and experimental work in the laboratory. Hurd arrived as the hospital was about to open and became at once a potent factor in its development, profoundly interested as he was in the new trend of medicine and highly gifted with keen literary tastes and attainments which proved invaluable from the very first in regulating and maintaining the standards of the numerous publications of the new establishment. He influenced the new hospital and the growing school in so many ways that it is almost impossible to do full credit to his work, which often took the form of a fostering daily guidance rather than of innovations. And then there was Osler, fresh from the stimulating atmosphere of the University of Pennsylvania, debonair, sparkling, energetic, enthusiastic, and ever delving in our English classics. A born scholar and yet working continually hammer and tongs at practical medicine, he rapidly threw up the vast superstructure of the departments in medicine and the medical school,

here, too, placing the principal emphasis upon pathology and the laboratory.

Osler and Welch, the most conspicuous men in the medical faculty of the Hopkins in the public eye, formed a remarkable and agreeable contrast. Welch, easily the leader in American medicine today, reminds one of Benjamin Franklin of a century and a half ago with his extraordinary breadth and catholicity of interests. He is, with Garrison, undoubtedly the best posted medical historian in the English-speaking world, endued as he is with a phenomenal memory and a gallic charity in his presentation of any subject that interests him, coupled with a poise and practical sanity rarely seen, and yet withal perhaps a little ponderous. With these attainments Welch stands out as the father of medicine in the young twentieth century.

Osler, on the other hand, with his keen incisiveness and vivacity, ever alert and refreshing himself at the fountains of his inspirations, became the master-builder of the fortunes of the new medical school which soon drew students from all over the land and visitors from every country; into these he poured his own spirit and then sent them forth like missionaries to extend the field of his operations and to enhance his fame. Osler and Welch thus admirably offset each other by their complementary qualities, each adding enormously to the effective work of the other.

But let us not forget as we do homage to these leaders the group of younger enthusiastic workers who used to foregather in the nascent school in little bands around their respective chiefs. There were Lafleur and Thayer and Barker in medicine, Flexner and Councilman and Abbott in pathology, and in gynecology a splendid coterie—an enthusiastic household of *dii minores* destined in their turn later to become *majores*.

The published contributions of Osler's men formed a distinct epoch in our medical literature and set a new pace for all our institutions. He organized the Lannaec Society to study tuberculosis and secured the Phipps Clinic for practical work in the dispensary. It was at this time, too, that the beneficent book and journal club was started on its career.

But let us not dwell so much upon these material and measurable contributions to medicine as upon the spirit of the workers, the disinterested affectionate mutuality of interests in which all the work was undertaken, in the generous desire to lead medicine out into new and fruitful paths, with the great investigators of the past as their models.

The spirit of these earlier days was taken up and fostered in the next generation by Mall, Howell and Abel, Meyer, Howland and Janeway. It seems to the writer, who would emphasize this side of the Hopkins Hospital life, that just in so far as the school has lived up to this spirit of her early history, just to that degree has she been successful. This refers not to any trammels of methods, nor to aught that can be formulated in a creed or crystallized in resolutions, but rather to an inner guiding spirit which, unconsciously adapting itself to all varying conditions, forgets self in the love of truth and zeal for suffering humanity.

As one who stood near to these master-builders and who claims the high merit of appreciating their work and worth, as one who drew daily inspiration from familiar intercourse and who yet lived somewhat detached, observant and not uncritical, I feel like saying of those early days when Osler was in his prime, and Welch and Halsted and Hurd were young, in the language of the most authoritative book in the world: "There were giants in those days. . . . the same became mighty men which were of old, men of renown." Let us hope and let us pray that neither they nor their descendants may ever fall from their high estate.

Osler is the type of man whom the world at large as well as our profession admires the most, the laughing philosopher with something of the bizarre about him, who, while he gaily floats in his little craft down the stream of time, discoursing sententiously on his favorite themes, "equanimity," "serenity" and "imperturbability," yet, being a man of affairs, keeps his hook out over the side of the boat and from time to time startles his rapt audience by pulling up from the deep a big fish for their delectation. In Osler the South has renewed her best traditions of the past.

MEDICINE

INTERNAL DISEASES, PEDIATRICS, NEUROLOGY, DIAGNOSTIC METHODS, ETC.

ANGIONEUROTIC EDEMA: A PRELIMINARY REPORT

By Charles R. Austrian, M.D.,
Associate in Clinical Medicine, Medical Department, Johns Hopkins University,
Baltimore, Md.

It is the purpose of this preliminary communication to emphasize the thesis that angioneurotic edema is a symptom and not a disease, and to show that in those cases in which the immediate cause of this manifestation can be discovered and removed, the symptom can be relieved.

Angioneurotic edema is characterized clinically by the occurrence, often periodic, of transient local swellings more or less circumscribed in the skin, mucous or synovial membranes. In typical cases they develop abruptly, are pale, painless, without evidences of inflammation and are accompanied by disturbances the nature of which depends upon the site of the reaction. Eosinophilia is commonly present and other evidences of vagotonia are more or less constantly found, i. e., erythemata, cold sweating palms, salivation, epiphora, increased gastric secretion, spastic constipation, pollakiuria, etc. In some cases there is a personal or a familial history of eczema, urticaria, hay fever or asthma. In many there is an associated psychoneurosis or a neuropathic tendency and occasionally purpura, Meniere's disease or migraine are met with in the same individual. Often there seems to be a family tendency to the syndrome (Osler). The condition occurs at all ages, but develops most often in adult life; more frequently in men than in women and especially among the financially well-to-do.

The differential diagnosis from edema of other origin will not be considered here.

There is no unanimity of opinion as to the underlying cause of the condition. Variously attributed to a vasomotor neurosis with suddenly increased local permeability of the vessels (Quincke); to a rise of lymphatic pressure due to the presence of an excess of lymphogogue in the circulation (Heidenhain, Lodor), or to a vasomotor or angioneural ataxia dependent upon disturbances of the autonomic nervous system (Solis-Cohen), the etiology of such states has not been discovered nor has the wherefore of its occasional familial transmission been given.

That angioneurotic edema is a symptom in the same sense that jaundice or albuminuria is, and that the specific excitants of it are at least several are shown by the following reports:

CASE REPORT

Case I.—H. S., aet. 22, December 20, 1916.

Complaint.—Itching and swelling of scrotum.

F. H.—Father and mother living and well. One brother living and well except for speech defect. Mother is of a neurotic temperament. No history of similar trouble in the family—no urticaria, hay fever, asthma nor idiosyncrasy to any food or drug.

P. H.—General health good. Measles and varicella in childhood. Grippe and otitis media at the age of 18, followed by impairment of hearing in the left ear. Intestinal taeniasis in January, 1916. The parasite (t. saginata) was recovered in its entirety and repeated stool examinations since then have failed to show the presence of ova or of segments. The patient has had no other illnesses. He has never had eczema, urticaria, asthma nor hay fever. He smokes 20 to 40 cigarettes daily and eats rapidly at irregular hours.

P. I.—About six hours ago an itching sensation developed in the pubic region and two hours later when examining himself for the cause of his discomfort the patient noticed that his scrotum was tremendously swollen. On being questioned, the patient recalls that during the past several days he has had evanescent itching swellings on the forearms, and this morning there was a painless, white swelling of the upper lip. Apart from the foregoing there have been no symptoms.

P. E.—The patient is a large, moderately obese young man. Height 6 feet. Weight 213 pounds (in clothing).

Eyes, nose and throat negative. Slight deafness in left ear. No general glandular enlarge-

ment. No signs of disturbance of thyroid secretion.

Thorax well formed, deep. Lungs clear. The heart is not enlarged. Action slow and regular. Sounds are of good quality and clear. Pulse 70 to the minute; regular in force and rhythm, and is of good volume and tension. Vessel wall not thickened. B. P. 125/80 (Tycos).

Abdomen: negative. Rectal examination, negative. Deep reflexes, normal.

Genitalia.—There is a soft, pale edema of the scrotum so marked that the penis is almost obscured. The penis itself is not involved. On palpation, the cushion of edema is so thick that the testicles are felt with difficulty. The swelling is painless and soft, but pits very little on pressure. Dermographia is present.

Urine Examination.—Clear, yellow, acid, sp. g. 1020 to 1014. No albumin nor sugar. Microscopic examination, negative.

Gastric Analysis (Ewald meal).—40 c. c. recovered. Free HCl, 60 acidity per cent.; total acidity, 85 acidity per cent.; no occult blood nor lactic acid. Microscopic examination, negative.

Blood Examination.—The flesh blood is of good color, flows freely, clots promptly, and on microscopic examination shows no abnormalities. R. B. C., 4,980,000; W. B. C., 8,800; Hb., 97 % (Sahli). Differential count, a normal formula except for a slight eosinophilia (5 %).

Stool Examination (following purgation).—Unformed stool; no mucus, blood nor pus; no parasites nor ova.

December 24, 1916.—The swelling of the scrotum subsided within 12 hours following the use of Tinct. belladonnae min. v, t. i. d., p. c., but recurred yesterday, when it lasted for 2 hours.

December 29, 1916.—This morning on awakening, the tongue began to swell and within 20 minutes it had become so large that speech was impossible. The patient attributed the symptom to the fact that he had eaten lobster salad before retiring. Examination showed the right half of the tongue to be so greatly swollen that it protruded through the lips, deflecting the tip to the left and posteriorly as far as the left canine teeth. The swelling was tense and painless. Following the hypodermic administration of 6 min. adrenalin chlorid solution (1-1000), the edema subsided sufficiently to permit of speech, although articulation was still interfered with.

January 1, 1917.—Careful search for a focus of infection disclosed none and the only result of pharmacodynamic tests was to show a tolerance for belladonna and for adrenalin. The patient was, therefore, tested to see if there were any evidence of sensitization with the protein of the common foodstuffs.

January 2, 1917.—Intradermic injections of extracts of milk (1 %), egg-white, chicken and beef gave negative reactions. Today there was atypical edema on the dorsa of hands and feet.

January 3, 1917.—Intradermic injections of extracts of oyster, lobster and of fish caused slightly greater reactions than the controls. The patient left the city at this time and was not seen again until August 10, 1917. During this period there were numerous swellings of hands, feet, lips and eyelids occurring at intervals of 2 to 1 days, always relieved by the injection of 6 min. of adrenalin chlorid.

August 16, 1917.—Intradermic injection of extract of fresh ham (unsalted) gave rise to a very marked local reaction with an indurated wheal six times the size of the control and a blotchy erythema that spread almost to the shoulder. This reaction reached its height in 45 minutes and a nodule 1.0 cm. in diameter persisted for 36 hours at the site of injection.

The reaction to ham was so definite that it was determined to proceed no further with the tests, but to learn what—if any—would be the result of withholding it and its congeners from the diet. Accordingly, all derivatives from the pig were forbidden the patient. This was the only change made in the diet; no medicines were prescribed and no symptoms developed until November 24, 1917.

November 24, 1917.—During the past two weeks, while traveling in the North, the patient adhered to his diet, but yesterday he ate an omelette with bacon and to this he attributes the present attack. He likewise states that when he eats food fried in lard he develops small swellings on the hands and feet.

In June, 1918, the patient decided to join the Marine Corps, but before applying for enlistment tested himself by eating several slices of ham. The reaction was prompt, leading to the development within the day of a marked edema of the entire face.

March 5, 1919.—Since June, 1918, there have been no major attacks and only twice have small swellings appeared on the dorsum of the hands, and these followed the ingestion of food cooked with ham fat.

This patient presents the typical syndrome of angioneurotic edema. The symptom is plainly the result of sensitiveness to ham. That the condition in this instance is an allergic one is evidenced by the idiosyncrasy to the food ingested, the local reaction that develops when the extracts of ham are injected into the skin and the absence of the symptom when ham or other products derived from the pig are abstained from. The only evidence needed academically to establish the existence of true allergy is the production of passive sensitization in another host by the injection of blood or serum of the patient. This test was not carried out.

The foregoing case is not a unique instance. I have studied four similar patients, one of whom reacts in like fashion to white beans, another of whom is sensitive to fish, another to veal, and a fourth (less well studied) to strawberries. The last case offers the same difficulty as do those suspected of sensitiveness to other fruits, berries and to tomatoes, namely, that satisfactory non-irritant extracts have not been procurable.

PREPARATION OF TEST MATERIALS

The solutions used in carrying out the tests in this patient and in all of the cases studied were prepared as follows: The material to be extracted was divided into small bits, placed in a sterile test tube and extracted with sterile water for 24 to 48 hours at body temperature. It was then filtered through a fluted filter paper and diluted to such a strength that the precipitation with 10 volumes of absolute alcohol caused an opacity equal to that of a 24-hour culture of B. typhosus in broth. Such a standardization is very crude, but after an experience with accurately standardized solutions in which determinations of the *N* in milligrams per cubic centimeter were used as the index of protein concentration, it was found to be satisfactory and to yield reliable results. Absolute sterility of the solutions is not necessary if they are to be utilized the day of preparation; but as a routine all extracts except those of egg white, which are coagulated by heat, were kept in boiling water for two periods of 30 minutes each.

TECHNIC OF TEST

The tests are made as follows: The flexor surface of the forearm is cleansed with alcohol and 0.05 c. c. of the various solutions are injected into the skin. It is necessary that the solution be introduced intradermically and not subcutaneously. In every series of tests a control test must be included and for this an equal quantity of distilled water or of 0.85 % salt solution is used.

INTERPRETATION OF THE TEST

A positive reaction is manifested by the development of a local wheal, elevated and tense with a pale center and a surrounding areola of blotchy erythema, either or both of which must greatly exceed that developing about the site of the injection of the control fluid. A response to be considered significant and specific must be at least 100 % greater than the control. Rarely the wheal may measure as much as 80 mm. (the injection nodule 3-5 mm.) and the erythema may spread over two-thirds of the arm. Associated subjective symptoms are common. The immediate pain or burning at the time of injection is without significance, but tingling, itching or paraesthesia following at an interval afterward is suggestive. A positive reaction is evident usually within 30 minutes: the maximum reaction may be delayed for several hours and not infrequently an infiltrated nodule persists 24 hours or longer.

In some individuals a marked reaction of nearly equal intensity develops about the site of injection of all the solutions, including the control, and in these it is unwise to infer the existence of a specific sensitization. The result is to be interpreted rather as an evidence of reaction to trauma and of vasomotor paresis in the same sense as is a dermographia or factitious urticaria.

The development of a typically positive reaction is evidence of a specific sensitiveness to the protein causing the response, and the effects of withdrawal of that protein from the diet of the individual confirm the idea that this substance is the immediate provocative cause of the appearance of symptoms.

CASE REPORT

Case II.—Mrs. C. H., aet. 43, white, female, May 5, 1919.

Complaint.—Hives and swollen eyes.

F. H.—Father died of heart disease. Mother died of "Bright's disease." No history of eczema, urticaria, asthma nor idiosyncrasy to foods or drugs. Entire family is nervous and high strung.

P. H.—General health is good. She has never been ill in bed except following a nephrectomy for tuberculosis of the kidney four years ago. Always energetic, over-active physically and mentally. Has never had urticaria before. No history of asthma, hay fever nor idiosyncrasy to foods or drugs.

P. I.—For the past four months the patient has had daily attacks of urticaria. The eruption recurs each evening at about 7 o'clock and lasts into the night, and then disappears. Associated with each efflorescence of the urticarial eruption there is swelling of the eyelids. There have been no visceral symptoms. General health remains excellent—appetite and digestion normal and there has been no relation of the symptoms to the food ingested. The cutaneous manifestations recurred with regularity even when the diet was limited to milk and water.

P. E.—The patient is a tall, well nourished, restless woman. No exophthalmous, extra ocular movements normal. There is marked edema of both upper eyelids and slight chemosis without evidences of inflammation. There is slight tremor of the fingers, and the palms are sweating. There is no struma, but there is tachycardia—pulse 120 per minute. Moderate dermographia. No general glandular enlargement.

Thorax well formed. Lungs clear throughout. Heart, not enlarged. Action rapid and regular. Sounds of good quality and clear.

Abdomen negative. Operative scar in right lumbar region.

Deep reflexes active. The skin is normal.

Gastric analysis, examination of the urine and stool were negative. Wassermann reaction negative. Goetsch test (adrenalin chlorid test) negative. There was a slight leucocytosis (11,000), but the formula was normal.

During the period of observation the patient relaxed and the pulse assumed a normal level (75 to 85 per min.).

Intradermic tests with water, 0.85 % salt solution, rye, wheat, egg, milk, timothy, orchard grass, poplar and beef showed a marked reaction to all, so no further tests were made.

Although there was no evidence of dental disease the teeth were examined roentgenographically and four periapical abscesses were discovered.

Note.--A report from this patient received June 12 stated that four days after the infected teeth were removed the symptoms disappeared and they have not recurred since.

In a similar case (C. S., aet. 78) following the removal of eight infected teeth, with simultaneous treatment of extreme pyorrhea alveolaris, the cutaneous manifestations disappeared and have not recurred in fifteen months.

The subsidence of symptoms following the removal of foci of infection warrants the inference that the infection was the proximate cause of the clinical manifestations, for no medication was given and there were no changes made in the dietary or in the patient's mode of living. Whether the protein of the infecting organisms or the interaction products between the organisms and the host are responsible entirely for the symptoms in this group of cases, or whether the symptoms develop only in those in whom there is an antecedent latent vasomotor neurosis, is a matter for speculation. The frequency with which foci of infection exist and the relative rarity of angioneurotic edema in such individuals seem to indicate that the infection is merely the immediate excitant of the symptom. No systematic efforts have been made in these cases to determine the presence of a sensitiveness to the proteins of various bacteria, but the use of such a procedure might throw some light upon the existence of an allergy, specifically due to a given bacterium.

Upon such evidence as the foregoing and upon the basis of other established facts, angioneurotic edema is considered one manifestation of at least several types of disorder. For convenience the syndrome may be subdivided on the basis of the proximate cause into the following types:

1. Allergic or anaphylactoid.
2. Infectious.
3. Endocrine.
4. Thermic.
5. Metabolic.
6. Idiopathic.

Type 1 is styled allergic because of the fact that in the patients included in it specific sensitization can be demonstrated by:

a. The development of the symptom-complex when the protein or proteins to which the individual is sensitive are ingested;

b. The demonstration of a specific reaction when the particular protein is applied dermally or intradermally; and

c. The abeyance of the symptom when the offending protein is withheld.

Type 2 is termed infectious on less secure ground. However, the fact that a local focus of infection is present and that the removal of the infection leads to a subsidence of the symptom is very suggestive. Doubtless the infectious group is really a sub-group of Type 1 and the sequence of events is probably infection, sensitization with the parenterally introduced protein of the invading organism or with the interaction products formed as a result of infection, and subsequent intoxication, with the efflorescence of symptoms. Securely to establish these cases as allergic, it is necessary to demonstrate at least a local sensitiveness to the protein of the offending organism, a test the need of which was not foreseen in the three cases of this type studied.

Type 3, the endocrine group, has been recognized by many observers. The frequent association of other evidence of vasomotor neurosis and the occasional occurrence of angioneurotic edema in Grave's disease are well known. The appearance of the syndrome at the climacteric, at puberty and in relation with the menstrual periods, suggest the influence of the internal secretion of the ovary. Finally, the disappearance of the symp-

tom in hyperthyroidism following operation and in some (2) cases at the menopause after the prolonged administration of large doses of ovarian extract, is confirmatory evidence and indicates that hyper-function of the thyroid gland and hypo-function of the ovaries (internal secretion) are more than casually related to the development of Quincke's syndrome. Doubtless the influence of the other ductless glands is of importance as well. Inasmuch as there is a familial tendency to dysfunction of these glands as well as to the development of angioneurotic edema, it would be interesting to study cases of familial angioneurotic edema for evidences of endocrine disease with the idea of testing the hypothesis that the familial types of the syndrome are of endocrine origin, a theory supported by the study of Hertoghe.

The thermic group, Type 4, includes the rare cases in which the typical syndrome follows exposure to cold. Cases of this type are described in the literature, but no satisfactory explanation of their origin is given.

The metabolic group, Type 5, comprises the cases in which the appearance of the symptom-complex is dependent upon a disorder of metabolism. Miller and Pepper (*Arch. Int. Med.*, 1916, xviii, 551) studied a patient with angioneurotic edema in whom during the attacks of swelling there was a retention of nitrogen, a reduced elimination of sodium chlorid during the three or four days preceding the maximum reaction, and in whom a low chlorid intake had a beneficial effect on the attacks of edema. We have observed one patient in whom there is a retention of sodium chlorid preceding the appearance of edematous swellings and who is symptom-free on a reduced intake of salt. The studies in this case, however, are incomplete and it is not yet certain whether or not an impaired renal function may play a role in this case as admittedly it may in the case reported by Miller and Pepper.

The idiopathic group, Type 6, is really no group at all, but includes those cases in whom no proximate cause for the symptom has been found. Further study will steadily diminish the number of patients so classified, registering them as members of one of the classes already recognized or of groups as yet undifferentiated. These patients have no demonstrable foci of infection and show no specific allergy. This group includes, among others, individuals in whom attempts to determine the existence of sensitization by intradermic tests, elicit reaction to many or to all of the test solutions. These reactions are non-specific, the result of trauma, and are simply evidence of an angioneurosis. In such patients it is fallacious to conclude that there is general sensitization with numerous proteins and to withdraw from the diet the many substances incriminated by the tests. Of course, such cases are to be differentiated from those in which there may exist an idiosyncrasy (in the sense of allergy) to several or more proteins, and this may be done by comparing the suggestive reaction with that developing about the site of the control injection, or, in the case of cutaneous tests, about the simple abrasion of the skin. Each individual with angioneurotic edema is a problem unto himself and only careful, often elaborate, study will determine to which type he belongs.

The facts presented warrant the conclusions that the etiology of Quincke's edema is not unitary and that the edema is a symptom of a vasomotor or angioneural disturbance.

These observations are very incomplete because the relative infrequency of the syndrome necessarily limits the experience of any one observer and they are published at this time with the hope that others may be stimulated to investigation along similar lines.

CHRONIC NEPHRITIS AND GOUT: CLINIC OF MAY 19, 1919, AT PETER BENT BRIGHAM HOSPITAL

By Henry A. Christian, A.M., M.D.,
Physician-in-Chief, Peter Bent Brigham Hospital; Hersey Professor of Theory and Practice of Physic, Medical Department, Harvard University,
Boston, Mass.

This patient (P. B. B. H. Med. No. 10973) is a young Greek. He is 27 years of age and has been in this country for a little over five years. Previous to 1917, he had frequent attacks of tonsillitis, and in February, 1917, he had his tonsils removed. In 1917, his right great toe became swollen and extremely sensitive, so much so that the weight of the covers of the bed would cause extreme pain. This attack lasted about two weeks. In 1918, he developed another attack in the same toe. There has been occasional sensitiveness in the left great toe. About three weeks ago he developed a third attack in the right great toe. This attack was not so severe as previously. We see that, beginning in 1917 down to the present time, he has had three attacks of pain in the great toe. When he came into the Hospital at this time, on April 29, his right great toe was moderately swollen and sensitive. With that swelling and sensitiveness he practically had no fever. His temperature has fluctuated some, but it has varied from sub-normal to normal. His highest temperature was 98.6°, the average being 98°, so he has not had any febrile reaction with that swelling in the toe. His pulse has been normal, averaging between 70 and 90; respirations 20. His weight and urinary chart you can see as it goes around. There is rather a decreased amount of urine. His renal history presents the other feature in the case.

Two years ago he noticed that his feet became swollen and in the mornings his eyelids would be somewhat puffy. He has been bothered a good deal with a dull headache every day and would tire very easily. He consulted a local physician at that time, who told him that he had acute nephritis. He then went to the Massachusetts General Hospital where he remained from May 8 till June 29, 1916. Just after leaving the Hospital he noticed on one occasion that his urine was somewhat bloody. For one year following that he did no work; he did not remain in bed but was up and about during this time. He suffered occasionally from a dull headache. In February, 1917, he went to the Massachusetts General Hospital again and remained there for thirty-five days. Following that time at no period has he felt well. His occupation is that of a barber. About a month ago he contracted a cold, and about this time his left great toe became slightly swollen and sensitive. (That is the third attack to which I have already referred.) The tenderness was marked, causing him a great deal of pain, even when he was not moving the foot.

His condition at the Massachusetts General Hospital was this: he was admitted on May 8, 1916, and was described as being well developed and well nourished. His lower eyelids were somewhat puffy. There was nothing abnormal in his lungs. His heart was normal. There was a very soft systolic murmur heard in the pulmonic area, not transmitted. The liver was felt 4.5 cm. below the costal margin. His spleen was apparently enlarged. A diagram from their record shows a mass in the region of the spleen measuring 14 by 8 cm. One can not make out from the diagram whether that is the size of the spleen that could be felt or whether it is a combination of the percussion outline and what was palpated. He had a low renal function at that time and blood and pus in his urine. He had an increased total non-protein nitrogen, it being 73 mg. on the 29th of June, 1916 (see Table 1). He was readmitted to the Massachusetts General Hospital on February 3, 1917. His spleen was then described as being palpable, hard and firm. The liver was described as being not enlarged. The liver dullness was from the fourth rib to the costal margin. At that time he underwent a tonsillectomy, as I have already said. On February 24, 1917, he had a blood-nitrogen of 136 mg.; on March 6, 1917, it was 76 mg. His urine at that

time contained from a trace to a large trace of albumin and a few granular casts; at other times no notes of casts were made. There was nothing abnormal about his blood.

Soon after that he came to our Outdoor Department and we have these notes on him: On March 26, 1917, his 'phthalein was 17 %. On April 2, his blood urea nitrogen was 56 mg., which does not show very much relative change from the preceding estimation of the total non-protein nitrogen; that drop in figure does not mean a decrease, the larger figure being the total non-protein nitrogen and the small figure simply the blood urea nitrogen. In the summer, July 30 of the same year, his 'phthalein was 15 %, and on September 27 of the same year his blood urea nitrogen was 66.5 mg. Then he came into the Hospital on April 29, 1919, and we got these figures: April 30, in four hours and five minutes the 'phthalein was the faintest possible trace. He was unable to urinate at the usual time and we did catheterize his bladder and so on that account have the long duration of the test. There was practically no 'phthalein. The blood urea nitrogen was 163 mg., and on a day or so later 151 mg. On the 7th of May the 'phthalein was a trace, the blood urea nitrogen 148 mg., and on the 14th the 'phthalein was again a trace, the blood urea nitrogen 182 mg., and on the 17th the blood urea nitrogen was 215 mg. On the 14th his blood CO_2 was 16.8 and on Saturday, the 17th, it was 15. During this time that he has been under observation in the Outdoor Department and here in the Hospital, his urine has not contained any very large amount of albumin, just a slight trace or a trace. Sometimes the examination showed no casts at all, and at other times a few casts were seen. For instance, early in April, the 2d of April, 1917, he had a rare granular cast and a rare fatty cast. In September, 1917, he had numerous red blood cells, but there is no note in regard to casts in that examination. (Those notes are from the Massachusetts General Hospital records.) This Spring, April 30, 1919, he had a rare red blood cell, numerous white blood cells, no hyaline casts and no granular casts. On the 1st of May he had a rare red blood cell, very numerous white blood cells and rare granular casts. Most of the examinations show the same thing, occasionally there is a rare hyaline or rare granular cast. In most of the examinations, except those that I mentioned, there were no red blood cells, but nearly always a considerable number of white blood cells. Fat droplets have been present; sometimes rare, sometimes numerous ones, in these various examinations. His blood picture is one of very moderate anemia, 4,200,000 red on April 30, 1919; no leucocytosis.

TABLE 1.

Date	Non-protein Nitrogen in Blood	Urea Nitrogen in Blood	'Phthalein Excretion in 2 hours and 10 minutes
June 29, 1916	73 mg.		
Feb. 5, 1917	160 mg.		
Feb. 24, 1917	136 mg.		12 %
Mar. 6, 1917	76 mg.		
Mar. 26, 1917			17 %
April 12, 1917		56 mg.	
July 30, 1917			15 %
Sept. 27, 1917		66.5 mg.	
Apr. 30, 1919		163.0 mg.	Trace
May 1, 1919		151.0 mg.	
May 7, 1919		148.0 mg.	Trace
May 14, 1919		182.0 mg.	Faint trace
May 17, 1919		215.0 mg.	
May 19, 1919		217.0 mg.	

The figures that I have put on the board (see Table 1) show very marked disturbance in 'phthalein, very marked retention of blood urea nitrogen and accompanying that there has not been much albumin in his urine, but always some, and there have been occasional red cells and abundant white cells. There have been few or no casts, occasionally a rare granular cast was seen and a moderate but varying amount of fat. There has been free fat and also fat on the casts.

Mr. Loh, what did you find in his abdomen?

Mr. L.: About 1 cm. below the xiphoid in the mid-epigastric line I could just feel the liver. It is not much enlarged. The spleen is just barely palpable.

Yes, the spleen or something in the region of the spleen can just be felt. It is

quite evidently smaller than it is in the diagram which I am passing around, which represents what they found at the Massachusetts General Hospital the first time he was there in 1916, and does not agree with their description of the second admission when they said it could easily be felt. Now it is just slightly enlarged.

Mr. L.: He has a scar on his abdomen. His appendix was removed, Dr. O'Hare, was it not?

Dr. O'H.: Yes, last November. Somebody told him at that time that his whole trouble was due to his appendix and that he had no kidney trouble at all. They operated upon him. This was followed by persistence of the same symptoms that he had been having.

(To Dr. O'H.): As far as you know, was it a normal appendix?

Dr. O'H.: I do not know anything about it.

Anyhow, it did not cure the renal condition. His appendix was removed last November, but I do not know anything about that except what Dr. O'Hare has told you. In a cardiac way he is apparently normal, so we won't bother to go over that. His blood pressure is practically within normal range. He has not a high blood pressure.

Here are some pyelograms of his renal tract. With the history of bleeding and some rather queer granular cells that we have seen in his urine at times, we thought possibly there might be some renal condition other than nephritis. Nothing was found in his bladder. The ureteral catheter you see is in position on one side, but on the other side has not gone in; it is just curled up. Just why it did not enter the ureter I do not know. You see, it goes up in a normal way to the position of the kidney on one side, but they did not succeed in catheterizing the other side. There is the pyelogram with the opaque substance injected. With dilatation of the pelvis of the kidney the calices are possibly a little deformed, but not enough to justify any conclusion as to the existence of a lesion in the kidney on that basis. It is probably a normal renal pelvis. There is a good deal of variation of course in the shape, size and number, etc., of calices in the kidney, and unless you get a marked distortion of one, a marked flattening or marked disturbance of some kind, you can not say that the variations are anything more than within the limits of normal.

On account of the story of pain in his great toe we had x-rays taken of his feet to see if they would show any evidence of disturbance in the bones or in the tissues about the bones, and you see there is very little there that is abnormal. Here is the great toe showing a little irregularity. There is a little increase in the lipping, a little formation, I should say, of beginning exostoses at the end of the metatarsal bone and the metatarso-phalangeal joint end of the first bone of the toe. Then there is at this point a slight suggestion of an area of rarefaction, a slightly punched out area or something of that sort. It is very indefinite; there is nothing very distinct about it. I think you can see that when you come down close to it, just in the base of that bone and in the base of the same bone of the great toe on the other side. There is a little suggestion of a punched out area at the distal end of the metatarsal bone, but there is nothing very distinctive nor characteristic in the bones of the toe to explain these recurring attacks of pain.

In that connection I think there are some determinations of his uric acid which are increased. It was 6.7 mg. on May 1, 1919.

Mr. Loh, what do those figures mean, blood CO_2 15? Today it was 21.

Mr. L.: I think it is somewhat increased; it ought to be about 8.

He would be in a pretty serious condition if it were 8. It ought to be considerably higher than that — 35, 40, or 45. He has a marked reduction in his blood CO_2. He has had some alkali in this interval. The increase to 21 may be the result of some alkali that he has had. I am under the impression that possibly the alkali was started before the first observation, a certain amount of alkali having been given before that.

What does a low blood CO_2 indicate?

Mr. L.: It indicates some increase in acids—acidosis.

What sort of acids increase in the blood? I do not mean particularly in him, but in general when you get low blood CO_2, what do you think of?

Mr. L.: Betaoxybutyric acid.

You get betaoxybutyric acid or some of its by-products. Ordinarily when you find a low blood CO_2 you have increase in the acids and the common ones to increase is the group of split products from the food fat, fatty acid of some kind, betaoxybutyric acid, diacetic acid or acetone. In some cases you find definite reactions for acetone and definite reactions for diacetic acid in the blood plasma, and if you quantitate you find that betaoxybutyric acid is present in increased amounts and with that increase, as Mr. Loh said, the patient has acidosis. The common condition in which we get acidosis is diabetes. This patient has no diabetes, no glycosuria. A patient with a figure as low as 15 for the CO_2 in his alveolar air or in his blood with diabetes is pretty close to the line of coma. Some of our cases almost in coma show a figure approximately that. If they go much below that with diabetes the patient ordinarily goes into coma and once they have gone into coma they do not come out of coma, so that your normal of 8 would be almost a terminal event in a case of diabetes. This patient has not diabetes and that low figure for his CO_2 is in relation to the renal disturbance as are those figures for his blood urea nitrogen and for his non-protein nitrogen. They represent retained acids rather than the acids of abnormal metabolism as in diabetes.

I wanted to put those figures on the board and show you the patient in connection with them and particularly call your attention to those increased figures for nitrogenous substances in his blood back in 1916. He has always had those high figures since then. Corresponding to that when the 'phthalein has been done, he has had a very low figure for 'phthalein, there was a trace of 'phthalein in all observations since admission. I do not know just what his 'phthalein was further back.

Did you have any 'phthalein figures earlier than those, Dr. O'Hare?

Dr. O'H.: No, we lost sight of him for a long time.

The first figures we have are 17 % in the last of March and 15 % in April, 1917, in our Outdoor Department, and when he reappears at this time there is practically no 'phthalein. I want you to contrast to that the other picture of not any very large amount of albumin in his urine, but albumin always present, often in moderate amount. There were few casts and not much history of edema, 'though in some of the notes he was said to have some swelling of his hands and some swelling and puffiness of his face, etc. There is no edema now beyond a very slight pitting over his tibiae. He has had the swelling and pain as described in his toe, but that is a different matter. Then there is the fact that his blood pressure has not been abnormal. There are a good many rather unusual and rather peculiar features in this case in just those respects. For instance, his blood pressure early in 1917 ranged between 112 and 138; then during the Summer of 1917 it was 126, 122 and 128 at different observations. At present, it is running lower than that. When he came in it was 122; on the 2d of May, 116; about the middle of the month, 94 and 104; and in the last two or three days it was down to 90 systolic, and the diastolic is correspondingly low. In the last record it was 90 systolic and 52 for the diastolic. There is no hypertension, no marked albuminuria, no edema, no very marked disturbance in the cellular part of the kidney as shown by casts or cells with the exception of pretty numerous leucocytes at the present time. At times there have been a good many red blood cells, at other times none, and in a good many examinations just a rare red blood cell. The patient is not febrile.

That is rather a different renal picture from that which one ordinarily gets. In the first place those low figures for renal function—the increased nitrogen back in 1916-17 has followed right along, indicating that the function has been getting poorer and poorer, the figures gradually increasing, until at present you get these very high figures for the blood urea nitrogen. The patient has been relatively in good condition. I do not mean by that that he has been well, because he has not; he has not been able to work, etc., but as

we see him now his nutrition is quite good. He has symptoms, for instance, of toxicity. He has had nausea and has vomited several times. This morning the nurse thought that he was a little bit more drowsy than he had been, but he is pretty far from being a boy in coma or anything suggesting coma. He is interested in his x-ray plates, interested in his examination, interested in you and is pretty different from the expected picture of a patient with as high blood urea as that (215 mg. on May 17 and 217 mg. today), as low 'phthalein as that and as low blood CO_2. Furthermore, apparently there has been a considerable period of time in which that renal function starting low has been getting poorer. It is over a period now of three years that he has had such figures, indicating a very steady progression downward of his renal function as shown by the figures for 'phthalein, of which, unfortunately, we have not very many, and rising figures for the blood urea nitrogen or total non-protein nitrogen, whichever was determined in the blood, without the signs of any very active degenerative or destructive process in the kidney as shown by any urine examination, and without, as I have already emphasized, high blood pressure, without edema or without cardiac failure.

The other thing of interest is in regard to his toe as to whether it is gout or not. We have never been able to find any tophi in him and I do not think you can say from those x-ray plates of his toes that that is or is not gout. Like most of the x-ray plates, they are non-committal as far as the evidence of gout is concerned. They show no evidences of uric acid deposits unless the small areas of increased density which I referred to might indicate a place where there is a certain amount of deposit of urates, but that is very questionable. You see that in a good many different plates and I do not know exactly how to interpret it. Looking at it in an antero-posterior direction, there might be scooped out areas on this surface, as far as the bone is concerned it being scooped out and filled up with deposits of urates, but if so, one would expect to get more evidence of it in a profile view. In this particular view when you come down you will see a little scooping out here and a suggestion of it there that corresponds with those joints that were painful. As far as the clinical history goes with the attacks limited to the toe, and very marked pain, out of proportion to the redness and swelling and out of proportion to the febrile reaction, it is very typical of gout. As a matter of fact, it is so typical of gout to have a great deal of local disturbance and little disturbance generally in the body, that I think most of the textbooks of medicine tell you cases of gout do not have fever or have very slight fever, but like many descriptions in textbooks it is not always true, because we do see very typical cases of gout with tophi, etc., which run a considerable amount of elevated temperature; 'though usually they do not have much febrile disturbance, whereas in contrast to that is the picture of acute articular rheumatism, where, if they show much local disturbance, there is a very much more marked general disturbance as represented by fever, so this boy's attacks are very typical of what is described as gout. The x-rays you may say possibly suggest it, certainly do not definitely rule it out nor definitely rule it in. That figure (6.7) shows a uric acid increase. The question is as to whether that helps us at all in the diagnosis of gout in this patient. What do you think about that, Mr. Loh?

Mr. L.: I think it helps.

The normal uric acid of the blood should not be over a few mg. per 100 c. c. This is much increased from the normal. The normal figure only goes as high as 4.5 mg. What abnormal conditions have high uric acid?

Mr. L.: Gout.

Yes, what else?

Mr. L.: Conditions of impaired renal function.

What is this—high uric acid from gout or high uric acid from a bad renal condition?

Mr. L.: I do not know.

That is not particularly a disproportionately high uric acid with those figures for the rest of his non-protein nitrogenous substances. I do not know about his uric acid in these early attacks when his renal function did not show such high figures,

but with that renal condition you can not say whether that uric acid retention is a part of gout or part of the renal insufficiency. What you can say is that it is not surprising to get that figure with his evidence of renal impairment; in fact, you would expect to get that figure with these others. With the blood urea nitrogen away up above 150 mg. you expect a marked increase in the uric acid. You do not have to bring in the diagnosis of gout to explain that high uric acid. If he were otherwise normal and the renal function showed normal tests, with a uric acid of 6.7 mg. and a blood urea nitrogen of 12, 13, 14, 15 or 16 mg. you might say that as far as the blood went there was strong evidence that he had gout. We have had cases of gout who had a high uric acid in which the uric acid increase was quite out of proportion to any disturbance of renal function. On the other hand, there are a group of investigators who think that the uric acid is the most difficult of the protein substances to excrete and consequently is the one first retained in renal insufficiency, that a high uric acid is the first indication of disturbance in renal function and that uric acid goes above normal before the other protein substances do, so there are difficulties in regard to diagnosis on that point. Anyhow, there is no question as far as this patient is concerned that he has symptoms suggesting gout. Further, there is no question that this uric acid figure is in perfect keeping with his disturbance leading to retention even if he did not have gout.

What sort of kidney has this boy got with those figures? He can not have the usual type of small granular red kidney with a good deal of arteriosclerosis in the renal vessels and a corresponding high blood pressure because so far as we can judge his vascular system is not particularly abnormal. His blood pressure is normal, now it is sub-normal, so it does not fall into the ordinary group of chronic interstitial nephritis, so-called. These nitrogen figures are not at all out of keeping with that diagnosis, but he lacks the high blood pressure and the vascular disturbance. Cases of that group, when they show these figures for blood nitrogen, however, ordinarily have had some signs of uremia. They have twitchings, convulsions, are stuporous or something of that nature. He does not belong to the other extreme with a very large kidney, which we ordinarily speak of as chronic parenchymatous nephritis or chronic glomerular nephritis, because he has not a large amount of albumin and has not an abundant sediment of casts and cells and has not edema, which are the typical accompaniments of that type of kidney lesion and those figures that we have here for 'phthalein and blood urea nitrogen are not typical of that type of kidney except in those cases that have progressed into a markedly atrophied kidney in which we have a combination of connective tissue increase and marked lesions in the glomeruli. We have seen such cases show figures of this type for 'phthalein and retained nitrogen, but ordinarily when that happens that case shows an increased blood pressure. You probably recall the little girl with the marked edema that Dr. O'Hare demonstrated to you and subsequently Dr. Wolbach showed you. That type of patient usually progresses faster than this patient has. They do not give a story going over three years of markedly low renal function.

Looking at this from the viewpoint of the physiology of the kidney without any reference to the question of nephritis nor to the question of the type of kidney that this boy has, I think one can figure out certain things. First, one can say that is a kidney that excretes very poorly. It excretes 'phthalein very poorly and it accumulates the nitrogenous substances that it should excrete. One can say further that there is not any element of inflammation in the sense of any active process, infiltration or degeneration or anything of that kind going on as far as the urinary picture shows. It simply seems to be something that blocks the excretion. It is not, in other words, a bit different from that which one would get if one took an animal and tied a string about both ureters and watched the blood urea go up. (Of course one could not do a 'phthalein test under those circumstances.) It is not very different from that which is seen in some cases where instead of complete occlusion

of the ureter there is some pressure on it that causes partial occlusion with piling up of the blood urea nitrogen, but some excretion of urine and in that urine small amounts of 'phthalein are excreted.

With that in view we recently studied the ureters in relation to the urethra and bladder, thinking possibly there was some obstruction, that possibly it was a case of hydronephrosis and with the hydronephrosis there was marked atrophy without any very adequate function left in the kidney, and that it had gone on so that the cortex was reduced to a thin layer with a lot of connective tissue in it and the tubules and glomeruli had, in large part, atrophied. In cystoscopic and catheterization studies there was no evidence of that. The same kind of process occurs in polycystic kidney where the kidney is greatly enlarged because of innumerable cysts of all sizes with connective tissue increase in the kidney substance between the cysts while the tubules and glomeruli are atrophied. Furthermore, the cysts themselves cause pressure on the tubules, and interfere with the urine's passing through the tubules, and in that way a mechanical factor is added. The cysts themselves are supposed to originate from mal-development of the kidney in which the normal junction between the lower and upper part of the kidney does not take place, and if there are a great many cysts there must be a great many tubules not functioning, and in all those ways there is disturbance along these lines of retention. This boy's abdomen is soft, easy to palpate, and one can not find any mass on either side of the abdomen such as one would expect with a polycystic kidney, so that diagnosis is eliminated. The fact that they could not get the ureteral catheter to enter on one side may indicate some obstruction such as a stricture. I do not know about that. Suppose it does; one kidney obstructed would not produce this picture because the other kidney would do the work. So, accepting that evidence as indicating that there is not proper drainage of one kidney through the ureter, still one could not explain the renal function on that basis because there is a normal pelvis on the other side, no obstruction, the ureteral catheter entering without any difficulty. There may be a mechanical obstruction on one side, but we have seen cases with complete obstruction of one ureter or congenital absence of one kidney, or something of that nature, and the other kidney do all the work satisfactorily. So none of these things explain this picture. We are therefore reduced to the idea of a very slowly-progressing sclerosing process which has caused a very marked injury of both the glomeruli and tubules, and at the same time causing no active inflammatory process.

Then we must assume that this has gone on without any of the ordinary association of retention of toxic substances or whatever they are that produce the manifestations of what we call uremia. Of course, in most cases with this sort of renal function, there is a great deal more of a picture of toxicity than this boy has. This boy's symptoms are more suggestive of what happens after the unfortunate surgical experience of removing one kidney or by mistake tying the only ureter existent, which happens sometimes, and there results an anuria, the piling up of these substances, a little discomfort in the way of headache, a certain amount of nausea, but there can be quite a long period of complete anuria without any severe toxic symptoms. In other words, this boy has something of that nature, coming on not over days but over a long period of time. It brings up the other question as to whether with this long history he might not have gotten readjusted to the accumulation of these toxic substances that, when retained, ordinarily cause a good deal of trouble, but to which this particular boy has become accustomed. One must always consider adjustment to toxic retention which has been going on for a long time. A brain tumor when of small size, growing rapidly, may cause marked symptoms, whereas when the brain tumor has grown slowly, to be of large size, it may give much fewer pressure manifestations. Adjustment there comes in and that may be a factor here.

The striking thing here is the poor renal function over a long time, the good condition of the boy and the absence of toxic symptoms. That is a progressive process of long duration and it is getting

worse. Now it has nearly reached the end stage with death certain in a short time. I should say that probably he has a very much reduced renal excretory tissue and probably the process is pretty uniformly distributed throughout the kidney, that it is a pretty uniform type of atrophy affecting all parts of the excretory mechanism and was never in any sense of the word an acute process unless one takes this history of hematuria on one occasion in 1916 as pointing to some severe injury and then the thing quieted down to a slowly-progressing process, causing very extensive atrophy of renal tissue and relatively little change in blood vessels outside the kidney. It is a very different case from the ordinary type of chronic nephritis.

May 26, 1919.—The patient that I showed last Monday with nephritis and marked retention has not made any particular change in the week. Though he has lost ground markedly, there has not been any very striking change in symptoms.

May 28, 1919.—The patient became increasingly stuporous. For a day and a half his breathing was slow and very deep. His vision became very dim 'though ophthalmoscopic examination showed no eye changes. He had no convulsions and remained conscious until 15 minutes before death. He died at 2:30 p. m. May 28, 1919.

THE MECHANISM OF NATURAL AND ACQUIRED IMMUNITY TO THE PNEUMOCOCCUS IN MAN*

By Paul W. Clough, M.D.,
Associate Professor of Medicine, Medical Department, Johns Hopkins University,
Baltimore, Md.

Intelligent prophylaxis and treatment of any infectious disease necessitates an accurate knowledge of its etiology and pathogenesis. Not only must the infecting micro-organism be known, but we must know how it gains access to the body, how it leaves the body, and how and where it maintains itself outside the body of the infected individual. We must ascertain the conditions which favor the development of infection after exposure has occurred, and how the body is injured by the infection. We must also know the mechanism by which the body wards off infection, or, if infection has occurred, by which immunity and recovery are brought about. In lobar pneumonia the conditions are peculiarly complicated, and it is only recently that we have reached an understanding of some of the fundamental facts concerning the disease.

It has long been recognized that the pneumococcus is the cause of nearly all cases which are clinically typical lobar pneumonia. There has been a great difference of opinion, however, as to the manner in which the disease is contracted. This has been in part due to the fact that in a considerable percentage of normal human beings, pneumococci are present in the mouth and throat which are not distinguishable culturally from those found in the lung in acute lobar pneumonia. The question naturally arises: why do not these individuals who harbor pneumococci in their mouths all develop pneumonia? It is because the organisms they carry are different in some way from those which cause disease? Are they less virulent, and is the development of pneumonia dependent upon the acquisition of a virulent strain of pneumococcus from an outside source? Or does pneumonia develop because of some reduction in individual resistance to infection which enables the pneumococci which have been leading a saphrophytic existence in the mouth to gain a foothold in the lung and give rise to an actual infection?

Definite evidence as to this fundamental point has been obtained but recently by a very thorough study by Cole and Dochez and their associates of the serological and immunological reactions of pneumococci from various sources. They have shown that pneumococci may be divided into four groups or types on the basis of their reactions to immune serum. Of these four groups, three represent distinct clear-cut types. The different strains of organisms belonging to each of these three groups are identical with one another in their serological reactions, but differ absolutely

*From the Medical Clinic of the Johns Hopkins Hospital.

from those strains belonging to a different group. Because of the clear-cut differences between organisms belonging to different types and the constancy with which these differences are maintained, they are frequently referred to as the fixed types; and they have been arbitrarily designated by Dochez and Gillespie[1] by the numbers I, II and III, according to their relative frequency as a cause of pneumonia. In Group IV are included all forms which are culturally pneumococci, but which do not fall into one of the first three groups. Most of the Group IV strains thus far studied differ serologically from each other as well as from members of the three fixed types. This group, therefore, represents a heterogeneous assortment of, for the most part, serologically unrelated forms, although recent studies[2] have shown that several minor groups may be differentiated among them.

Exhaustive studies of the relative frequency of these various types of pneumococci in lobar pneumonia have been made at the Rockefeller Hospital[3] and their results confirmed in many other clinics in this country. These studies have shown that between 60 and 70 % of all cases of primary lobar pneumonia are due to pneumococci of Types I and II, which are of nearly equal frequency; that about 15 % are due to Type III strains (pneumococcus mucosus); while between 20 and 25 % of the organisms concerned fall into Group IV.

In addition to the serological differences between these types, certain other differences have been made out, which are of the greatest epidemiological significance. Pneumococci of Types I and II, which cause nearly two-thirds of all cases of lobar pneumonia, are usually highly virulent for animals. Furthermore, they cause a high mortality in man, approximately 33 1/3 %. While organisms belonging to these two types may be present for several weeks in the mouths of patients convalescent from pneumonia, they have been found but very rarely in the mouths of normal individuals, except in those who have been in intimate contact with patients with pneumonia of these types.[4] They do not seem adapted to a saprophytic existence in the mouth. It seems certain, therefore, that pneumonia due to organisms belonging to Types I and II can rarely be autogenous in origin, but, as in typhoid fever, the infection must be acquired from an outside source, i. e., from a patient with pneumonia or from a healthy carrier recently in contact with a patient. It is strictly a communicable disease, although only to a slight degree contagious.

On the other hand, pneumococci belonging to Group IV and also the so-called Atypical Type II pneumococci described by Avery[5], are usually of relatively low virulence for animals. The mortality in man (except for terminal pneumonias in patients with chronic disease) is also low, about half that of Types I and II. It is mainly organisms of these groups which are found in the mouths of normal individuals. It is, therefore, possible that pneumonias of these types may often be the result of an autogenous infection; and this supposition is strengthened by the frequent finding by Clough[6] of Group IV and Atypical Type II pneumococci in postoperative pneumonias, and in terminal pneumonias in patients debilitated by alcoholism or chronic disease, and by the frequency of Group IV pneumococci as the cause of post-influenzal pneumonia.

Type III pneumococci are peculiar in that they are usually of high virulence for animals, and yet are frequently found in the normal mouth. Although they are a relatively infrequent cause of pneumonia, the mortality in these cases is high, about 60 %. No definite differences have been demonstrated between the strains found in normal mouths and those isolated from patients with pneumonia, either in serological reactions or in virulence for animals. It would seem, therefore, that the normal human body must possess a considerable power of resisting the establishment of infection with Type III pneumococci, but has less power of combatting and overcoming an infection once established than in the case of infection with pneumococci of other types. It also suggests that there may be some difference in the mechanism of resistance to infection with pneumococci of different types. From an epidemiological standpoint, each type of pneumococcus must be regarded as a dis-

tinct species, and receive independent consideration.

The problem of the resistance of man to pneumococcus infection is a double one, and concerns both resistance to the establishment of infection, and ability to overcome an infection which has been established. The former may be called natural immunity, the latter acquired immunity. Since the phenomena associated with acquired immunity in general are more striking and therefore more easily recognized than those of natural immunity, more attention has been devoted to the former subject, and more is known concerning it. A knowledge of the mechanism of such an acquired immunity may be directly helpful in the study of natural resistance, since the latter may depend upon factors which can be more readily demonstrated by the study of acquired immunity.

It has been shown that recovery in pneumonia is not associated with any change in the consolidated lung tissue which is detectable by physical examination or by the x-ray. It is not due to any loss of virulence nor other demonstrable change in the infecting organism. Definite changes, however, have been found in the serum of patients at or near the crisis. It has been shown by a number of observers[7] that the serum at this time possesses the power of protecting mice from infection with otherwise fatal doses of highly virulent pneumococci, provided one uses in the test the strain of pneumococcus with which the patient was infected, or at least a strain of the same type. These findings have been confirmed by some observations of the author[8]. In my experiments the degree of protective power was much less marked than that exerted by serum from highly immunized animals, but varied from 10 to 10,000 times the M.L.D. Serum obtained from the same patients during the acute stage of the disease showed no protective power, nor did serum obtained from patients who subsequently died of the disease.

Numerous attempts have been made to determine the mechanism of this protective power. It was at first supposed to be due to an antitoxin, analogous to diphtheria antitoxin, but subsequent studies have not confirmed this view. It was next attributed to bactericidal substances in the serum, which act directly upon the microorganisms, but this view also has been disproven. While normal human serum, as shown by several previous observers,[9] and confirmed by the writer, often exerts a marked inhibitory action upon the growth of pneumococci as tested by plating methods, this action is not increased in the serum of convalescent patients. Furthermore, this phenomenon is a transient one, and pneumococci after a latent period will usually grow quite readily, either in normal or in immune serum.

The explanation was next sought in an increase in the opsonins in the serum, and a number of observers reported finding an increase in the opsonic index for pneumococci at the crisis. However, the errors inherent in the method make the reported results questionable, and, even if accurately determined, it is doubtful if a rise in opsonic index has any significance. In determining the opsonic index of a patient's serum by the ordinary method one uses a strain of pneumococcus of feeble virulence which is moderately phagocytable in normal serum, quite without reference to the type of pneumococcus with which the patient was infected. Even if there were an increase in the phagocytic activity of the serum for such an organism, this would not necessarily indicate any increase in resistance to highly virulent strains of the fixed types which are resistant to phagocytosis in normal serum.

That phagocytosis plays an important role in immunity to the pneumococcus, however, is well established. If virulent pneumococci are injected into the peritoneal cavity of an immunized animal, the organisms are ingested by the leucocytes and undergo death and intracellular digestion within the leucocytes. Multiplication of the pneumococci does not occur, and the animal recovers, apparently as a result of this phagycytosis. In a normal (susceptible) animal, on the contrary, the organisms remain extracellular, multiply without restriction and death of the host speedily follows. If an avirulent strain of pneumococcus is used, however, even in the normal animal, the organisms are in-

gested and destroyed by the leucocytes, just as were the virulent organisms in the immunized animal. If the dose is not overwhelming in size the animal recovers. This power of causing phagocytosis of the injected pneumococci is dependent upon the presence of some substance in the serum, which can exert its activity in the test tube as well as in the body. Thus, if we mix in the test tube equal volumes of a culture of virulent pneumococci, leucocyte suspension, and immune serum, the pneumococci will be ingested and dissolved. In a corresponding mixture containing normal serum, no phagocytosis will take place. An avirulent or feebly virulent strain, however, will be phagocyted in fresh normal serum. There is roughly, at least, a fairly close parallelism between the virulence of a pneumococcus and its resistance to phagocytosis in normal serum.

Attempts to demonstrate phagocytic activity for highly virulent strains of pneumococci in the serum of patients have been hitherto almost uniformly unsuccessful. However, little attention was paid in most of these experiments to the type of pneumococcus with which the patient was infected.

A few years ago the writer[8] demonstrated such phagocytic activity in the serum of a small number of patients taken after crisis for the homologous strain of pneumococcus. This finding was confirmed by Lister[10] in South Africa. The writer has recently reported the results of a further study[11] of a series of 40 cases of lobar pneumonia in which the phagocytic activity of the serum in each case was tested with the homologous strain of pneumococcus which was isolated from the patient whose serum was being tested, and also with other strains of pneumococci of the same type, and of different types. In 85 % of the patients who recovered, the serum at or after the crisis or lysis showed well marked phagocytic activity for the homologous strain of pneumococcus, and as a rule for other strains of the same type, whereas it was quite inactive toward pneumococci of different types. The serum of these patients during the acute stage of the disease was quite inactive, as was the serum of all but one of the patients who died. This phagocytic activity was equally well marked in patients recovering from infection with virulent pneumococci of Types I, II and III, and with the less virulent forms belonging to Group IV. In a smaller series of cases the writer[8] had previously shown that there was a parallelism between this phagocytic activity and the capacity of the serum to protect mice. Furthermore, in the body of the protected mouse, as in the test tube, phagocytosis and intracellular digestion of the ingested organisms took place. It, therefore, seems probable that this property which the serum had acquired of causing phagocytosis of the virulent pneumococci with which the patient is infected plays an important role in the immunity which develops in man at crisis.

Agglutinins have also been demonstrated in the serum at crisis by a number of observers, notably by Chickering,[12] and his findings have been confirmed by the personal observations of the writer.[11]. Furthermore, Blake[13] has shown that the serum at crisis very frequently, although apparently less constantly, contains specific precipitins, similar to those present in immune serum.

Very possibly other unknown activities of the serum may be concerned. In any case, it has been shown clearly that the serum of patients recovering from pneumonia in most instances has acquired in some degree those properties which are manifested much more actively by the serum of immunized animals, and there can be little doubt that this activity of the serum is one essential factor in recovery.

It seems quite certain, however, that other factors are concerned than the activity of the serum. This has been pointed out particularly by Cole[14] on the basis of his experimental work, especially on the fact that while a small amount (0.2 c. c.) of potent immune serum will protect mice from a dose of 0.2 c. c. or less of a highly virulent culture of a Type I pneumococcus, no amount of serum will protect from doses of culture much larger than this. Some unknown factor must be supplied, in this experiment, by the tissues of the mouse, which is adequate if the infection is not too large, but which does not suffice if the infection is excessive, even

although a great excess of protective serum is present. The writer has observed one patient who died of pneumococcus sepsis, notwithstanding the fact that his serum shortly before death and after the onset of the sepsis caused well marked agglutination and phagocytosis of his own organism. Furthermore, in a number of other cases, I have found that organisms (belonging to Group IV) which were cultivated from the blood of patients who subsequently died of the disease, were readily phagocytable in normal serum.

One essential factor is probably the presence of an adequate number of active leucocytes. Winternitz[15] and his associates have shown that animals whose leucocytes had been reduced in number by benzol were rendered abnormally susceptible to pneumococcus infection. Clinically a low leucocyte count is an unfavorable prognostic sign in patients with a serious infection, although the reverse is not necessarily the case. We are not certain that the leucocyte of the circulating blood is the only cell concerned in phagocytosis, nor even the most important one. Doubtless the activities of other tissues are also essential.

The importance of these facts in the serum treatment of pneumonia has been pointed out by Cole.[16] The fact that in natural recovery from pneumonia the same antibodies are elaborated by the patient as are present in artificially produced immune serum, supports the assumption that recovery may be hastened by the therapeutic administration of such serum. The failure of such serum to protect animals from very large doses of culture emphasizes the importance of the early institution of serum treatment in Type I infections. It also explains in part the therapeutic failure of Type II serum, since this serum will not protect animals from as large doses of culture as will Type I serum. It seems probable that any further marked advance in serum treatment must await the discovery of the nature of these essential activities of the body tissues, and the elaboration of appropriate methods of stimulating them.

While our knowledge of the mechanism of recovery from pneumonia is far from complete, still less is known as to the causes of natural resistance to infection. The conditions may differ in detail, with pneumococci of different types. In the case of Group IV and Atypical Type II organisms, the forms usually found in normal mouths, there must be a comparatively effective means of resistance, and infection may be precipitated by a temporary disturbance which in some way lowers this resistance of the host. In the case of infection with organisms of Types I and II, which are rarely found in normal individuals, exposure to infection is essential; but here, too, a considerable natural resistance to infection must exist, since relatively few of those in contact with patients with Type I or Type II infection contract the disease, although, as shown by studies at the Rockefeller Hospital,[1] about one-eighth of the individuals so exposed become carriers of pneumococci of these types for an average period of 3 to 4 weeks.

Why do some individuals exposed to infection contract the disease while the majority escape? Is it because of differences in local conditions in the lung or differences in the antibacterial activities of the blood or tissues? We would be in a better position to answer this question if we knew exactly what happens between the entrance of the pneumococcus into the mouth and the development of the consolidation in the lung.

The consensus of opinion seems to favor the view that the organisms reach the lung by direct passage downward through the bronchi. It seems very probable that, in addition to the presence of the organisms, local changes in the lung play an important role in determining the development of a consolidation. The well known predisposing effect of chilling can most simply be explained in this way rather than by assuming that it reduces any protective powers which may be exerted by the blood or leucocytes. Meltzer[17] has suggested that local circulatory and secretory changes may be brought about by chilling, as a result of which the finer bronchi may be plugged with mucus, and thus a condition spontaneously be produced analagous to that of the lung distended with culture fluid in the experimental animal.

Some writers have advocated the view that pneumonia, like typhoid fever, is a general infection from the start, that the organisms reach the lung through the blood stream, and that the usual development of a local lesion in the lung is due to some especial vulnerability of that organ to the pneumococcus.

It is not impossible that both modes of infection may occur. In either case it seems probable that the activity of the tissues and of the blood constitutes an important mechanism of defense, which is defective or insufficient in those individuals who develop pneumonia. This would be particularly significant if we are to regard pneumonia as a general infection from the start.

In the case of the Group IV pneumococci present in normal mouths, phagocytosis is probably an important mechanism of defense. These organisms, even those isolated from patients with pneumonia, are usually readily phagocytable in fresh normal serum. In so far as one can draw conclusions from the results of animal experiments phagocytosis would offer a plausible explanation, although not necessarily a complete one, for the usual resistance to infection with these organisms. In the case of individuals who acquire the disease, there might be some transient reduction in this phagocytic activity of the blood, or the organisms might, as a result of special local mechanical conditions, penetrate into some region where they would be protected from this antibacterial action of the blood, and hence be able to multiply until a sufficient number of organisms had accumulated to overpower the defensive forces of the host and produce disease. A bronchus plugged with secretion might constitute such a focus.

In the case of virulent organisms of Types I, II and III, this explanation does not apply. These forms of pneumococci are usually entirely resistant to phagocytosis in normal human blood in the test tube experiments. That conditions in the body may be more favorable for phagocytosis is, of course, possible, but we have no evidence for such an assumption. That there is some defensive mechanism present seems highly probable in view of the existence of normal carriers of these strains, especially of Type III.

Since the immunity which develops with recovery from pneumonia is often associated with the appearance in the serum of definite protective power for animals, it seemed to the writer that a similar, although probably less marked protective power might be demonstrable with normal human serum, or with serum from those individuals who may possess a well marked natural resistance to pneumonia. It has previously been shown, particularly by Neufeld and Haendel,[18] that some specimens of normal serum may exert such protective power, but no systematic studies of normal serum have been reported.

The writer recently undertook a study of the protective power of normal human serum against pneumococci of Types I, II and III. All of the sera studied were from normal individuals who had not suffered from pneumonia recently, nor received pneumococcus vaccine. The cultures used were of very high virulence, one tenmillionth of a cubic centimeter killing the control mice regularly within forty-eight hours. The tests were carried out in the usual manner by mixing in a small syringe 0.2 c. c. of the serum and 0.2 c. c. of diluted culture, the actual quantity of the original culture varying from 0.01 to 0.0000001 c c. The mixtures were injected immediately. As a control a similar series of mice was injected with the same quantities of culture, but without serum. The mice were observed for ten days, and those surviving for this period were regarded as protected.

Serum from 20 individuals was tested in this way with each of Types I, II, III. Definite protective power was demonstrated in 4 sera for the Type I strain; in 8 sera for Type II; and in 8 sera for Type III. There was no one serum which protected definitely against all three types. Most of them protected only from one strain; 2 sera protected from Types I and II; and 2 from Types II and III. The degree of protective power in some was slight, 10 M. L. D. In others it was comparatively high—1,000, 10.000, and with one serum 100,000 M. L. D. These

figures compare favorably with the protective power of the serum from vaccinated or convalescent individuals.

That this protective power is not due simply to a direct injury of the organisms by the concentrated serum is shown by the fact that incubation of the mixture of serum and culture for one-half to six hours before injection did not increase the protective power, and especially by the fact that mice could be protected by subcutaneous injections of serum from subsequent intraperitoneal injections of organisms.

The mechanism of this protective action I was unable to determine. These sera caused no agglutination of the organisms against which they were active; nor could any appreciable degree of phagocytic activity be demonstrated. It was suggested by Neufeld and Haendel[18] that this protective power of normal serum might be due to its slight bactericidal properties. This point has been studied at my suggestion by Miss C. Van Winkle. While she also has been able to demonstrate that normal serum does apparently exert a definite transient inhibitory effect upon the growth of pneumococci of these types, this activity was no more marked in the sera which showed protective power than in those which did not. Attempts to demonstrate precipitins in these sera have also been negative. It would seem, therefore, that the mechanism of this protective power must be somewhat different from that of immune serum.

As to what the significance of this protective power may be, one must speak with the greatest caution. It seems very probable that it indicates a definite power of resisting pneumococcus infection. That it indicates a state of absolute security against infection is improbable. It may explain in part, at least, why individuals who harbor pneumococci of Types I and II in their mouths (contacts), and also those harboring Type III pneumococci do not more frequently develop the disease.

The assumption that this protective power of the serum indicates an actual resistance to the disease is strengthened by recent observations on the serum of vaccinated individuals. Attempts to produce immunity to pneumonia by the vaccination of human beings on a large scale have been reported by Lister[19] in South Africa and by Cecil and Austin,[20] and Cecil and Vaughan[21] in the United States Army. The production of an effective immunity is pretty clearly shown by the reduction in the incidence of pneumonia due to the types of pneumococci contained in the vaccine, among the vaccinated individuals. Lister demonstrated agglutinative and phagocytic activity in the sera of the vaccinated individuals similar to that which develops after spontaneous recovery. He found that this activity of the serum may persist for months. The American writers mentioned also found agglutinins in the serum of most of the cases examined, but made no observations as to phagocytic activity. They found that many of these sera also showed definite protective power for mice, most marked with pneumococci of Type I and Type II. The degree of protective power reported was about as great as that found by Dochez,[7] and by the writer,[8] in the serum of patients convalescent from the disease. So far as reported, specimens of serum from the same individuals, tested before vaccination, with one exception showed no protective power.

Undoubtedly other factors than the activity of the serum are concerned in natural immunity, as has been shown to be the case in acquired immunity. While this protective power of the serum, therefore, is probably not an accurate quantitative index of all the defensive forces of the body, nevertheless it is generally regarded, and probably rightly so, as the most reliable test of immunity now known which is applicable to man.

While our knowledge of the mechanism of acquired immunity in man is very incomplete, that of natural immunity is most meager. A more thorough insight into these processes is essential both for the elaboration of more efficient methods for the specific treatment of pneumonia, and for the institution of effective prophylactic measures to prevent the spread of the disease.

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A THERAPEUTIC STUDY OF BENZYL BENZOATE IN BRONCHIAL SPASM OR ASTHMA

By David I. Macht, M.D.,
Lecturer in Pharmacology, Medical Department, Johns Hopkins University, Baltimore, Md.

The writer has for a number of years been engaged in an extensive and intensive pharmacological study of opium, and more especially of the so-called "minor" opium alkaloids, individually and in combination with each other and with the principal opium alkaloid, morphin. As the result of that work, it soon became evident that the minor opium alkaloids can be regarded as "minor" only in respect to their small quantitative content in crude opium, but not in respect to their pharmacological action. Indeed, it was shown that these alkaloids can and do modify the effects of morphin very markedly when given in combination with it. Thus it was pointed out that there is a distinct difference in the analgesic effect produced by morphin, on the one hand, and by opium, on the other, due to the presence of the minor alkaloids in the latter.[1] Again, important differences have been shown to exist for the same reason between the pharmacological action of morphin and opium on the respiratory center,[2] the vomiting center,[3] and other centers in the medulla.

One interesting feature disclosed by the pharmacological studies just mentioned is the fact that while opium and its alkaloids exert their most marked effects upon the central nervous system, nevertheless they produce also distinct and important pharmacological effects upon peripheral structures, and more particularly upon smooth muscle organs. The action of the opium alkaloids upon smooth muscle was first studied by the author in connection with a pharmacological study of the ureter, because excised rings of that organ permit of an accurate analysis of the action of drugs upon the rhythmic contractions or peristaltic movements and the tonicity of smooth muscle.[4] It was soon established from studies upon the excised ureters of lower animals and of man, as well as from observations of the ureters in lower animals *in situ*, that the opium alkaloids in respect to their action upon that organ can be divided sharply into two classes: the pyridin-phenanthrene group, of which morphin is the principal member, on the one hand, and the benzyl-isoquinolin group, of which papaverin is the chief representative, on the other. The morphin group was found to stimulate the contractions of the ureteral preparations and increase their tonicity, while all the members of the papaverin group were found to inhibit the contractions of the ureter and lower its tonus.

It was found, furthermore, that in combinations of members of the two groups small amounts of the benzyl-isoquinolin class were sufficient to overcome the stimulating effects of the morphin group. These observations led to several practical deductions. Thus, at the suggestion of the author, Dr. J. T. Geraghty injected a solution of papaverin directly into the ureter of a patient and in that way facilitated the expulsion of a small ureteral calculus.[5] Again the tonus-lowering action of papaverin and its relatives gives a scientific explanation to the well-known empirical observation that opium is more efficient in relieving the pains of renal colic than is morphin when given alone, because when administering the combination of total opium alkaloids the patient has the advantage of both the central narcotic or analgesic effect of morphin as well as the peripheral tonus-lowering or antispasmodic influence of the papaverin group.[6]

Following the studies of the effects of the opium alkaloids upon the smooth muscle of the ureter, the author investigated the action of the same alkaloids upon other kinds of smooth muscle. The results of these investigations have been published elsewhere. The smooth muscle structures thus studied were the following: intestine, pyloric rings, uterus, gall-bladder, urinary bladder, biliary ducts, seminal vesicles, vas deferens, bronchial rings, and rings of excised arteries. As a result of these investigations the author was led to conclude that the action of the opium alkaloids upon all kinds of smooth muscle structures is the same as that described in connection with the ureter, namely, that the morphin alkaloids stimulate contractions and increase tonus, while the papaverin alkaloids inhibit contractions and lower tonicity, and, furthermore, that so far as the peripheral effect is concerned, in case of combinations of the two groups, the benzyl-isoquinolin constituents exert the predominating effect. Here, again, some practical deductions were drawn from the experimental data. Thus it was found, as has been long known by empirical observation, that opium is more efficient in relieving gall-stone colic and uterine colic than is morphin when administered alone.[7 8 9]

Following the experimental investigations just described, the author undertook a further analysis of the interesting peripheral action of the opium alkaloids, and especially of the alkaloid papaverin, upon smooth muscle. The results of these investigations have been published elsewhere.[10] Briefly stated, the conclusions to which these studies have led were that the stimulating effect of the pyridin-phenanthrene group of alkaloids is to be attributed to the pyridin portion of their molecules, while the inhibitory and tonus-lowering action of papaverin and the other members of the benzyl-isoquinolin group were to be ascribed to the presence of the benzyl grouping in their molecules. The reasons for these conclusions are to be found explaned in detail elsewhere.

These observations and conclusions led the author to surmise that possibly the inhibitory and tonus-lowering effect of papaverin might be produced by the exhibition of a benzyl grouping in a simpler form. Accordingly a search was made for simple non-alkaloidal and non-narcotic compounds containing the benzyl radical which could be administered to animals without toxic results. Two such bodies were discovered. They are the well-known esters, benzyl-benzoate and benzyl-acetate.[11] Inasmuch as these esters are practically insoluble in water, their pharmacological action could not be well studied upon excised tissues or isolated organs, but experiments with them upon intact animals revealed the fact that both of these esters actually produced the same pharmacological effects as those given by the opium alkaloid papaverin upon the one hand, and that these esters were much less toxic than papaverin upon the other. Metabolic studies in connection with these experiments showed that the benzyl group of benzyl-benzoate and benzyl-acetate is, in a large measure, converted in the body into hippuric acid and is excreted as such in the urine. The comparatively very low toxicity of benzyl-benzoate and benzyl-acetate for animals and their striking papaverin-like effects upon various viscera led the author to try their action upon himself, and as no untoward or even dis-

agreeable symptoms followed the ingestion of these drugs by mouth it was deemed justifiable to administer these agents to suitable patients with their consent.[12 13]

The conditions in which the benzyl effect was anticipated to produce therapeutic results were those exhibiting either excessive peristalsis or excessive spasm of smooth muscle. Such conditions could be readily thought of and were actually treated by the author with benzyl-benzoate with very satisfactory results. Among them may be mentioned: excessive peristalsis of the intestines, such as in diarrhea and dysentery; intestinal colic or enterospasm; pylorospasm; biliary colic or spasmodic contractions of the gall-bladder; uterine colic; ureteral or renal colic; vesicle spasm, etc. Among the most interesting groups of cases thus treated by the author were those exhibiting a bronchial spasm or "true asthma."

The term asthma, as is well known, is applied to a variety of conditions, all characterized by dyspnea. A large number of cases of asthma, however, are characterized by a spasm of the finer bronchioles. It is for this group of cases that the term asthma should properly be reserved. Even these cases of so-called "true asthma" are not an entity, and the etiology and pathogenesis of asthma are still in a state of hopeless confusion. In connection with a study of the anti-spasmodic properties of benzyl-benzoate on the smooth muscle organ, it was thought desirable to try its effect in cases of bronchial spasm. The results were so striking that a more careful study of the drug in this connection was undertaken.

CLINICAL DATA

Up to date the author has collected the records of over 150 cases of bronchial spasm or "asthma" treated with benzyl-benzoate. Most of these cases were treated under the author's own direction, but a certain number were treated by other physicians and the data were sent to the writer. The cases of asthma thus treated were both in adults and in children. Indeed, some of the most striking and successful results were obtained in the case of infants. Many of the cases in adults were of very long standing, the histories dating many years back. In many of the cases, all kinds of drugs, including opiates and epinephrin, were tried with very little success.

Benzyl-benzoate was administered in most of the cases by mouth and in a few cases by intramuscular injection of the drug dissolved in olive oil. The preparation administered by mouth was a 20 per cent. alcoholic solution. Of this the dose for adults was ordinarily from 15 to 25 drops in cold water three or four times a day. As benzyl-benzoate, when given by mouth, is practically non-toxic, much larger doses of the drug could be given with impunity but are not necessary. In the case of infants and children, the dose was proportionately reduced, but even in case of very young children, doses of 30 to 40 drops three times a day have been given without any untoward results. When the drug was to be given by injection, a few minims of either benzyl-benzoate or benzyl-acetate were dissolved in olive oil and the solution injected deep into the muscles. Pure benzyl-benzoate and benzyl-acetate are not adapted to injection as they are somewhat irritant. In most cases, however, injections are not necessary and all the therapeutic results can be obtained, if they are obtainable, by giving the drug *per os*.

RESULTS

An analysis of all the cases on hand reveals that the benzyl-benzoate treatment of asthma was beneficial in about 75 per cent. of the cases. In some of the cases the results were very striking and were equaled only by those obtained through injections of epinephrin. Furthermore, a number of cases, which failed to respond to epinephrin, were relieved by the administration of benzyl-benzoate by mouth. Curiously enough, however, a number of cases failed entirely to react to the benzyl treatment. This, however, was not very surprising, as the asthmatic cases include really a variety of different conditions, and where the dyspnea is due to other causes than the bronchial spasm, the benzyl-benzoate can be of very little

use. The following protocols will serve as illustrations of the cases treated with benzyl-benzoate:

Case 1.—J. E. N., a medical student, has been suffering for a number of years with severe asthmatic attacks. During one of his protracted spells, the patient was admitted to the Johns Hopkins Hospital. Ordinary treatment with drugs failed to relieve him. He was then given injections of adrenalin. These relieved the attacks for very short periods of time and had to be frequently repeated. At the suggestion of the author, all medication was discontinued, and the patient was given a 20 per cent. solution of benzyl-benzoate by mouth, 20 drops four times a day. A few doses of the drug were followed by a marked subsidance in the violence of the dsypnea, and two days later the patient left the hospital in pretty good health. The patient has asked for the drug a number of times since, whenever he began to suffer from these asthmatic attacks.

Case 2.—M. S., a boy 17 years old, was taken with a most violent attack of asthma in October, 1917. Injections of adrenalin failed to relieve him. Even morphin by mouth and hypodermically was followed by little relief. The patient was given an injection of benzyl-acetate, four drops in olive oil. This was followed by distinct amelioration of the symptoms. He was then given benzyl-benzoate by mouth and in a few days was comparatively well. In October, 1918, almost exactly one year after the previous attack, the patient was taken again with a violent spell of asthma. This was again ineffectually treated by the author with epinephrin, but was very quickly relieved by the administration of benzyl-benzoate.

Case 3.—L. J., female, colored, age 37, Johns Hopkins Hospital Dispensary, No. F93522. On May 3, 1918, the patient came to the Dispensary complaining of asthma. Examination revealed the typical physical signs of asthma, viz., wheezing respiration, dyspnea and numerous rales. A blood examination showed 13 per cent. of eosinophiles. The patient was given benzyl-benzoate 20 per cent. to take 20 drops three times a day. In a few days she returned, stating that the bad spells had stopped. She was continued on the drug until, in two weeks after the beginning of the administration, the asthma cleared up entirely.

Case 4.—Mrs. G., 30 years old. She has been suffering for several years with very acute attacks of asthma, which were not relieved by adrenalin and required morphin injections several times. The patient was given 20 drops of benzyl-benzoate four times a day and was improved more than by any other treatment. The blood examination showed 15 per cent. of eosinophiles.

Case 5.—Mrs. L. G. Z., 46 years old, was married and had no children. "Neurasthenia" 1908-1911; hysterectomy for fibroid in 1913; well nourished until attack of whooping-cough in 1916. The present illness, a very obstinate and severe form of asthma, dates its onset from the whooping-cough. The patient reacted to three proteins and sharply to dogs' hair; nasal polypi were removed, but were followed by little improvement in the asthmatic attacks. She was treated with epinephrin and was taking considerable quantities of codein. When first examined in November, 1916, by her physician, Dr. W. A. D., of New York, her physical signs were those of a moderate emphysema, varied of course by the signs usually found during asthmatic attacks. Several sputum examinations were all negative for tubercle bacilli. The heart was normal; blood pressure 140 systolic and 90 diastolic; urine normal. She was having daily asthmatic attacks coming on at 5 P. M. and lasting well into the night. The patient went to a sanatorium in December, 1916, where she at first improved, but later grew worse. During the month of February, 1918, she was taking ⅛ to ¼ grain of morphin sulphate nightly with some relief. After the first dose of benzyl-benzoate, 25 drops in water on the night of February 25, she expectorated a great deal of mucus and was relieved of her dyspnea. The relaxing effect of the drug upon the bronchioles, produced by the drug, at the height of a very severe attack of asthma, was especially emphasized in the local physician's report. After a few days of medication, the patient was much more comfortable, went down to meals frequently and even out of doors. There was certainly marked improvement in the condition. The latter history of the case is wanting.

Case 6.—Mrs. B., 57 years old. Case of Dr. D., of Baltimore. Has been suffering from repeated attacks of asthma which could not be relieved by ordinary medication. The patient was given benzyl-benzoate by mouth, 20 drops every four hours, and the asthma was completely "cured." Some time later, when another attack occurred, the patient begged for the same medicine and it was followed by prompt relief.

Case 7.—Baby K., 1 year old, was suffering from persistent asthmatic attacks. The attending physician had to administer opiates, but being loath to continue the narcotic treatment, requested the author to try benzyl-benzoate in this case. About 5 drops of the drug were administered three or four times a day. The relief was so prompt, following this administration, that the parents resorted to the same treatment several times during other attacks which occurred later.

Case 8.—Asthma in a girl of 19, who gave negative skin tests to all proteins, and whose asthma bore no relation to any known circumstances and resisted the ordinary treatment with calcium, with diet, with iodids, and other drugs. This patient was "cured" for the time being after taking two ounces of benzyl-benzoate solution.

Case 9.—Wm. J. D., 47 years old, carpenter. J. H. H. Gen. No. 118821. Severe asthma, rendering the patient incapable of work. Onset 9 years ago. Diagnosis of nasal polypi and bronchial asthma was made in Hospital. Excision of polypi and ethmoids was performed. No relief. Patient has been taking all kinds of medicine, without relief. Was referred to the author by Dr. S. J. Crowe. Given benzyl-benzoate 20 per cent. solution every four hours. Three days later he reported as being improved, though still asthmatic. Continued 30 drops every four hours.

A week later the patient says the drug helps. He expectorates more freely and can sleep at night. In this case there was a distinct amelioration of symptoms, but no complete relief.

The above histories will suffice as illustrations of the therapeutic action of benzyl-benzoate in "asthma." The number of examples could be multiplied, both from the author's experience and from data furnished by other physicians. Thus, for instance, a number of interesting cases have been reported to the author by Dr. Francis M. Rackemann, of Boston, and other cases of equal interest have been treated under the author's direction by Drs. Harry Goldberg, S. A. Dodd, Charles Austrian, A. Chatard, G. Woltereck, A. H. A. Mayer, and others of Baltimore; Dr. S. Solis Cohen, of Philadelphia; Dr. W. A. Dunckel, of New York, and by other physicians.

All the data so far in hand concerning the benzyl therapy of asthma seems certainly to show that benzyl-benzoate is an invaluable drug in the treatment of that condition. It should, however, be clearly understood that not every case of asthma is benefited by this drug, and this is not at all surprising. Indeed, in view of our lack of knowledge of the etiology and pathogenesis of asthma, that should be expected. It should be borne in mind in weighing the value of benzyl treatment in asthmatic conditions that its action is merely as a broncho-dilatator and sedative to the bronchial muscle. In other words, only those cases of asthma may be expected to yield to the effects of the drug which are characterized by a spasm of those structures. In such cases the experimental and clinical data described above bear ample proof that benzyl-benzoate is of great usefulness, and it is, therefore, hoped that that drug will prove to be a desirable addition to the physicians' rational therapeutic armamentarium.

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INTENSIVE ARSPHENAMINE THERAPY

By H. H. Hazen, M.D.,
Professor of Dermatology, Medical Departments of Georgetown and Howard Universities,
Washington, D. C.

At the present time there is no uniform method of treating syphilis. This is because we lack certain fundamental information: in the first place, we are still uncertain as to what criteria constitute a cure; next we are ignorant concerning the life history of the Treponema pallidum, for it may be possible that, as McDonagh suggests, there are forms that resist arsphenamine. In the third place, we are not sure just how the arsenical works; and lastly, we do not know the exact position of certain of the organisms in the tissues and just how long it takes the drug to reach them. It is possible that when surrounded by fibrous tissue the blood plasma may not work its way in for several days, and that by this time all of the arsphenamine has either left the plasma or exists in an inert form. Until more of these points are made clear we shall not have a truly scientific basis, but merely a clinical one, and at the present time the literature is woefully scanty on the subject of late results in the treatment of syphilis.

Only a few years ago syphilitic patients received but one to three injections of arsphenamine, but it soon became apparent that this was not sufficient and six injections at weekly intervals became a more or less fixed routine among many syphilologists. Then came the tendency toward giving another course following a period of mercurial injections. Three years ago Pollitzer first advocated the use of three injections of arsphenamine in as many days and other excellent men have followed and approved of this work, although there have been one or two dis-

Case	Age	Sex	Duration of Infection	Lesions.	Wass.	Previous R.	No. Injec.	No. Courses	Lesions.	Wass.	Late Result
1	36	M	3 years	Retinitis	++++	8 arsphen.	3	1	Well	—	Well 2 years, clin. & serol.
2	29	M	1 year	Latent	—	5 arsphen.	3	1		—	Recur 1 year later, clin.
3	33	M	3 weeks	Chancre	++++	1 arsphen.	7	1	Well	—	Well 1 year, clin. and serol.
4	19	F	5 weeks	Roseola	++++	1 arsphen.	8	2	Well	—	Well 1 year, clin. and serol.
5	26	F	Years	Latent	++	None 8 yrs.	3	1		—	Lost sight of
6	29	M	Years	Mucous patch	++	None 6 mos.	6	2	Well	—	Well 1 year, clin. and serol.
7	29	M	Years	Latent	+	None 6 mos.	3	1		—	Lost sight of
8	35	M	Years	Latent	+++	None 6 mos.	4	1		—	Lost sight of
9	34	M	Years	Latent	++	3 arsphen.	4	1		—	Lost sight of
10	34	M	Years	C. N. S.	—	3 arsphen.	4	2	Improved	—	Slight recur. one year
11	27	M	6 mos.	Papular	++++	None	8	1	Well	—	Lost sight of
12	47	M	Years	C. N. S.	—	None 1 year	7	2	Improved	—	Slight recur. one year
13	41	F	Years	C. N. S.	+++	Mercury pills	8	1	Improved	—	Slight recur. one year
14	46	F	Years	Periostitis	++++	2 arsphen.	3	1	Well	++++	Lost sight of
15	29	M	2 weeks	Chancre	++++	None	8	2	Well	+—	Lost sight of
16	49	M	Years	Arthritis	++++	1 arsphen.	3	1	Well	—	Lost sight of
17	28	M	1 mo.	Papular	++++	None	7	1	Well	—	Lost sight of
18	27	M	2 weeks	Chancre	?	None	5	1	Well	—	Lost sight of
19	24	M	1 mo.	Papular	++++	None	3	1	Well	—	Lost sight of
20	24	F	3 mos.	Macular	++++	1 arsphen.	5	1	Well	—	Lost sight of
21	32	M	4 years	Latent	++	Merc. inj.	3	1		—	Lost sight of
22	45	F	Years	Latent	++	None 1 year	3	1		—	Lost sight of
23	35	M	3 mos.	Papular	++++	None	4	1	Well	—	Clinically well 1 year
24	48	M	Years	Gumma tongue	++++	None	7	1	Well	—	Clinically well 2 years
25	26	M	1 year	Recur roseola	++++	6 arsphen.	6	1	Well	—	Lost sight of
26	19	F	3 mos.	Roseola	++++	1 arsphen.	3	1	Well	?	Lost sight of
27	27	M	2 mos.	Papular	++++	Mercury	2	1	Well	?	Lost sight of
28	23	F	6 weeks	Papular	++++	None	12	2	Well	—	Clin. and serol. well 1 year
29	63	M	Years	Myocarditis	++++	Mercury	4	1	?	?	Lost sight of
30	17	F	4 weeks	Roseola	++++	None	12	2	Well	—	Recent case
31	35	F	Years	C. N. S.	++++	4 arsphen.	12	2	Improved	—	Recent case
32	29	M	2 mos.	Papular	++++	None	14	2	Well	—	Recent case
33	27	F	1 mo.	Chancre	++++	None	9	2	Well	—	Recent case
34	54	M	Years	Tabes	++++	Mercury	6	1	Improved	—	Recent case
35	36	F	Years	Tabes	++++	None	6	1	Improved	—	Recent case
36	37	F	Years	Latent	++	12 arsphen.	9	2		—	Recent case
37	23	F	2 weeks	Chancre	++++	None	6	1	Well	?	Recent case
38	38	M	1 year	Recur. pap.	++++	6 arsphen.	6	2	Well	—	Lost sight of
39	25	M	1 week	Chancre	—	None	14	2	Well	—	Recent case
40	24	M	3 weeks	Chancre	++++	None	12	2	Well	—	Recent case
41	33	M	1 year	Latent	+	12 arsphen.	10	1		—	Recent case
42	26	F	1 mo.	Roseola	++++	None	9	1	Well	—	Recent case
43	28	M	3 mos.	Latent	++++	Mercury	4	1		—	Recent case
44	26	F	4 mos.	Latent	++++	Mercury	4	1		—	Recent case
45	29	M	1 week	Chancre	—	None	8	1	Well	—	Recent case
46	17	M	1 mo.	Papular	++++	None	8	1	Well	?	Recent case
47	39	M	Years	Latent	+	12 arsphen.	3	1		—	Recent case
48	29	M	Years	Latent	++++	6 arsphen.	4	1		?	Recent case
49	48	M	Years	Throat	++++	Mercury	3	1	Well	?	Recent case
50	56	M	Years	C. N. S.	—	Mercury	4	1	Improved	—	Recent case

senting voices. The Army regulations call for one injection every five days, obviously a compromise.

Two years ago I began by treating my private patients with injections given every three days, choosing this interval because most of the drug was excreted by the end of this interval and because any serious reaction should be manifest in time to avoid the dangers that might result from a further injection. However, the real object of shortening the interval between injections was a double one: first, to see if a considerable saving in time could not be effected; and second, to learn if more frequent injections were not more efficient. Of course it is realized that there can never be, in civilian life at least, a real routine treatment for syphilis, and this for the reason that no two patients are alike and that each individual must be carefully studied. The presence of early meningeal involvement, a complicating nephritis, loss of weight under treatment and many other factors must always be taken into consideration and the patient treated accordingly.

The technique of operation was simple: patients were given 0.4 gram of arsphenamine, Arsenobenzol brand, for each 150 pounds of body weight, the time of injection was not less than five minutes, freshly distilled and boiled water was employed. Sixty cubic centimeters of water was used for each 0.4 grams of the drug. All injections were given in the office and the patients were allowed to go home immediately afterward.

To date fifty patients have been treated by this method and a total of 309 injections have been given them. The highest number of injections given any patient was fourteen and the lowest two. The average course was either six or eight injections given at three-day intervals, although either a two- or a four-day interval might occasionally be employed to better suit the conveniences of the patient. In one case ten injections were given at a three-day interval and in another case nine.

In no instance did we see any jaundice or any evidences of renal irritation. In the florid cases there was usually a considerable reaction to the first injection, but the others gave no trouble. In two cases after the fourth dose severe urticaria developed, and before subsequent injections atropine was employed hypodermically as suggested by Stokes in cases where there was apparently an anaphylactic response to arsphenamine, the urticarial attacks being much lessened in severity. In both of these cases a two instead of a three-day interval had been employed. In all cases, bar one which was lost sight of and one in which there was no effect, the Wassermann reaction promptly became negative, this almost uniformly occurring within four weeks of the time that treatment was started. In every instance the clinical result was excellent.

Mercury was not used in conjunction with the arsphenamine. The reasons for this are as follows: experimental work has shown that the treponema gains a slight amount of tolerance for arsphenamine and a considerable amount for mercury, a tolerance that is soon lost. Hence, it theoretically seems best first to use one drug and then when a tolerance on the part of the organism is established, to shift to the other. In addition it is not unusual to find that patients tolerate mercury badly, and very rarely that the arsenical preparation is badly borne. If both drugs are being given at the same time it is impossible to tell which is making the trouble.

To sum up, it may be said that while the three-day interval is not advocated as the only method to be employed, or even as the ideal method, yet it has been demonstrated that a patient will stand as many as ten injections at seventy-two-hour intervals with perfect impunity, that much time is saved, and that both clinical and serological conditions are brought to normal in a much shorter space of time than is possible with injections given but once a week. So far as ultimate results are concerned, it is still too early to say just what will take place, but so far the observations are encouraging.

INTRODUCTION TO THE PRELIMINARY COURSE IN PHYSICAL DIAGNOSIS*

By William S. Thayer, M.D., LL.D.,
Professor of Medicine, Medical Department, Johns Hopkins University,
Baltimore, Md.

In nearly thirty years of teaching in this Hospital, the pleasantest and most interesting, and, I am sure, the most important work that I have had to do, has been the meeting of the third and second year classes at the beginning of their study of physical diagnosis. The way in which one approaches one's clinical studies is a matter of considerable importance. *"C'est le premier pas qui coute."* If the first step be a false one, if you begin as so many good fellows have begun in the past, with the feeling that all you have to do is to sit at the feet of a group of professors, whose wise enunciations you are to take as gospel, and to learn from books descriptions of symptoms, signs and diseases, and then to go forth and hunt for something that matches your mental picture, you will be fatally side-tracked. You will leave the institution with the feeling that your medical studies are over, and your greatest contribution will be to discover that the "type" of pneumonia or typhoid fever in the region in which you live has changed—changed forsooth from the mental picture you had carried from the class room. Ah, how full medical literature is of such communications!

If, on the other hand, you carry away with you a sense of obligation to put to proof so far as you can every statement with which you meet; if you carry away with you a reasonably good knowledge of the manifestations of disease based upon clinical experience and a familiarity through practice with the more important methods of physical examination, you will find stimulation in the very difficulties with which you meet. You will be an intelligent practitioner and maybe a contributor to the science and art of medicine. Most that you are going to learn, from now on, you will teach yourself. 'Tis our task to try to see that you start in the right way, that you make your own discoveries, work out your own problems and become in the proper sense a student of medicine and not a disciple blindly following the precepts of a book or a teacher.

During the past two years you have been giving your attention largely to studies in the laboratory of anatomy, physiology, chemistry, pharmacology and pathological anatomy. You are presumably more or less familiar with the structure of the human body, and with the nature of its normal functions, as well as with the gross and microscopical changes that occur in the commoner diseases. So far, however, you have not been called upon to determine in the living human being whether the anatomical structure and physiological functions correspond with the normal, nor have you been confronted with the problem of attempting to recognize in the living, deviations from the ordinary nor abnormalities and processes of disease such as you have studied in the pathological laboratory.

In the next three months you are going to familiarize yourself with some of the simpler methods by which you may recognize these deviations and abnormalities. Next year you will pass on to the application of what you have learned here to the diagnosis of disease in the living subject. After all, this is but a continuation of what you have been doing with Dr. Mall, Dr. Howell, Dr. Abel, Dr. Jones, and Dr. McCallum. Methods of examination would be useless to you had you not had a good basis in anatomy, physiology and especially pathological anatomy. A familiarity with the anatomical changes associated with disease is of vital importance. Indeed, one may safely say that the most important part of physical diagnosis you learn in the pathological laboratory. With the familiarity with pathological changes which you should have gained there, you would very possibly, if left to yourself, work out a good many of the procedures necessary for the detection of these changes in the living. History, indeed, shows that methods of physical examination were evolved step by step along with the advances of our knowledge of patho-

*Lecture to the second year class of the Johns Hopkins University School of Medicine.

logical anatomy. In 1760, Morgagni published his famous work on the "Seats and Causes of Diseases Investigated by Anatomy." Here for the first time was a systematic comparison between the history and symptoms of the patient during life and the changes observed in the organs at necropsy. Morgagni's work marks the beginning of pathological anatomy. Previously to that time the medical world in general had but the rudest conception of the changes which disease produced in the body, and the methods of examination of the patient during life were equally crude, but immediately following the work of Morgagni, appeared the publication of Auenbrugger, in Wien, describing "A New Method for the Recognition of the Diseases of the Interior of the Chest by the Percussion of This Cavity," the first description of this simple and vital method of physical examination, which depends upon tapping a structure to determine the sound elicited and thereby to gain information as to the physical condition of the underlying organs. A simple procedure, it seems to us today, yet it was literally discovered only about a hundred and fifty years ago. When Morgagni showed that certain symptoms of disease were associated with solidification of the lungs or accumulation of fluid in the pleural cavity, it was not long before acute physicians discovered accurate methods for detecting the existence of these conditions before death. It was not many years before a brilliant Frenchman, Laennec, had added an immense fund of information as to the character and significance of the sounds produced in the normal and diseased chest by the discovery of auscultation and his contribution to normal and pathological anatomy.

No physician who has not had a good experience in the pathological laboratory can be a good diagnostician. The best diagnosticians are those who most frequent the necropsy room.

What you are going to learn now are certain principles and methods and procedures of observation and examination of the living human being. The information which you will acquire from these procedures will be of little value, unless you have a clear idea of the nature of the pathological conditions with which you may be concerned. From the employment of purely physical procedures you will gain purely physical information. In a space which should be occupied by an air-containing body you will discover a solid or a collection of fluid. That is as far as you can go. What that body or what that fluid may be, no book can tell you. You can arrive at reasonable conclusions only by using your own common sense, acting upon the basis of the knowledge you have gained by your experience in the ward and in the pathological laboratory. You can not make an intelligent diagnosis of a pneumonic solidification of the lung if you do not know what a pneumonic solidification looks like, or the conditions under which it occurs, or the symptoms to which it gives rise. And after all, here the application of your common sense to medicine only begins. If any of you share the common fancy that medicine can be practiced by rule, you should rid yourself of it forthwith or abandon the idea of becoming a physician. It may be that in Heaven all things are regulated by rule, including the practice of medicine. Very fortunately for us mortals it is different on earth. If medicine could be practiced by rules; if life could be ordered wholly by fixed regulations, the function of the physician would be small, and life would be insufferably dull.

You are going to satisfy a competent board of examiners that you possess sufficient knowledge of anatomy, physiology, chemistry, pharmacology, as well as the methods of physical exploration, and the use of surgical instruments to be let loose upon the public. From that time on you are bound only by the rules of common honesty and decency. All that medical ethics and etiquette mean is common honesty and decency and consideration for your patient and your fellow practitioner. You must practice medicine as you make diagnoses by your common sense playing upon the basis of your real knowledge. He who practices medicine according to the directions of X's practice or Y's therapeutics should have been a homeopath: he is a puppet.

Why does a human being consult a doctor? For various reasons. Firstly, and

most commonly, because for one reason or another he becomes conscious of himself. The normal human being does not think about himself; he does not know how he "feels." He does not attempt to analyze the difference between his "feelings" on one morning and on another; and even if some one were to direct his attention to himself and ask him how he "feels" today as compared with the ordinary, he would probably be unable to answer; he does not "feel" at all; of himself and his normal functions he is unconscious. When, however, for one reason or another, he does become conscious of himself and his functions, sooner or later he becomes interested and often concerned, and thence it is but a step to the consultation of some one who may better be able to interpret the conditions that puzzle him. The complaints which bring the patient to the doctor may be simple and easily analyzable, or they may be difficult and almost impossible to unravel. 'Tis these difficulties and puzzles that make the practice of medicine fascinating to the man who is fit to be a doctor.

Secondly, a man consults a doctor because he has come to fear that something may be the matter with him, or because he wants assurance that he is sound and well. It may be that he is a nervously constituted individual who has heard somebody talk of a malady of some sort, the picture of which so obsesses him that he wants assurance that he is not a victim. It is not uncommon for healthy, vigorous, athletic young men between twenty and thirty to ask a physician for a complete physical examination. This is a symptom that is almost pathognomonic of a condition which is common, if not morbid. Nine times out of ten that man is contemplating matrimony.

You have then reached the point where you are confronted with the problem of the detection and definition of deviations from the ordinary or normal in the living human being. What are deviations from the normal? And how may they show themselves? What is the normal? These are questions which are often among the prettiest problems that a physician may meet. To solve them demands careful observation, practice and experience. 'Tis the only way. In a gross sense deviations from the ordinary may be physical (that is anomalies or abnormalities in the position or the size or shape of an organ) or functional, in the sense that the action of that organ produces different physical or chemical manifestations. The detection and the interpretation of these physical and functional deviations from the ordinary constitute the fascinating art of diagnosis.

And do not deceive yourself: diagnosis is an art which can be acquired only by training, long practice and experience. Diagnosis, then, is an art, empirical, if you will. The word empirical is used often as a reproach in connection with things medical. Medicine is "empirical," say the critics of the doctor, wishing thereby to indicate that the physician deduces his conclusions from his own fancies and prejudices, or from an experience interpreted by a mind which is not open, without regard to the teaching of science. But science derives its theories and its laws only from observation and experiment and the master whose ingeniously designed experiment, whose keen powers of reason lead him to formulate the theory or detect the law has become a master only through long training and study and experience. It is no insult to the art of medicine to say that it is largely empirical, that it is largely based upon the teachings of observations and experience. This is but to say the truth. The art of medicine as it comes more and more to be based upon scientifically established conclusions, theories and laws, becomes, 'tis true, less and less empirical. We are able to recognize many diseases today with a scientific accuracy which was impossible yesterday, but still in the interpretations of many of the signs of disease, as well as the effects of treatment where an exact scientific basis for a conclusion is wanting, we must still be empirics in the good sense of the word; we must still be guided by experiment and experience.

To the physician with a good scientific training and an open mind, experience is the main teacher and guide which makes of him a master in his art.

To another with an unsound foundation, experience may be useless.

To him who is ill-trained and possessed of a prejudiced mind (the man to whom all experience but tends to bolster a preconceived idea), to him experience may be dangerous.

What do we mean by physical diagnosis? Sometimes the terms "physical" and "functional" diagnosis are used as if they represented two separate and distinct procedures. In recent years, with the great increase in instruments of precision and the expansion of our knowledge of physical and chemical methods of exploration, the term "functional" diagnosis, especially, has come into common use. This division into physical and functional diagnosis is comprehensible, but not wholly sound. One might truly say that the determination of the size or position of the heart was a matter of purely physical diagnosis—that the determination of the quantity and rate of urea output in the urine, under fixed conditions of diet and general surroundings, was a matter of functional investigation. In a general way a division between physical and functional diagnosis may often be maintained; but in reality, physical and functional diagnosis are so closely bound together that they can not absolutely be separated. For instance, by the simple physical methods of exploration which are included ordinarily under the head of physical diagnosis, you can determine much concerning the normal or abnormal functions of the heart and lungs. The more complicated questions of functional diagnosis, as the term is commonly used, demand, however, laboratory studies and often experiment. In its proper sense the term physical diagnosis should be used purely with reference to the methods of exploration which are employed. This is the sense in which it applies to your work of this year and next. The methods with which you are to work in this course are purely physical procedures, which you yourself can practice in the consulting room and at the bedside of the patient with your five senses assisted by the simpler instruments of precision.

On your ability to use your five senses and properly to interpret the information they give you, depends your usefulness or your uselessness as a physician. No book can teach you physical diagnosis. The kernel of all diagnosis is observation; that you must make yourself. You can not reason safely on the description of another. The development of well equipped laboratories which relieve the physician in the city from the necessity of making his own examinations of the blood, urine and sputa, and the aid that the development of radiography, electrocardiography and other methods of physical investigation have brought to the physician have enabled us to study our patients much more accurately than we could thirty years ago.

Radiograms, electrocardiograms, tests of renal function, are of great assistance in establishing a correct diagnosis and prognosis—to the physician who can interpret them. But' tis well to remember that they are but single stones in the edifice of a diagnosis. They are of little help and may be misleading to one who can not interpret them. The man who fails to make, or is incapable of making an intelligent physical examination, is incapable of benefiting materially by such assistance.

The experience of the war has revealed a deplorable lack of knowledge of the basic principles of physical exploration in the medical profession of America. A surprisingly large number of officers were content, without reasoning, to accept a laboratory report as the basis for a diagnosis. To take one example, at one time a considerable number of soldiers were being returned to America with the diagnosis of pulmonary tuberculosis. Investigation of one hundred of these patients by an expert revealed recognizable evidences of tuberculosis in only about 30 %; the other 70 % represented, for the most part, convalescents from acute pulmonary infections. The reason for this was simple. Many of the officers dealing with these patients had blindly accepted an x-ray diagnosis of pulmonary tuberculosis. But upon what was such a diagnosis of tuberculosis based? Upon the presence of certain shadows which indicated changes in the lungs, very possibly in some instances the result of tuberculosis. This is not un-

usual. Think of necropsies that you have seen. How many individuals dying of typhoid fever, or cardiac disease, or anything that you may choose, show in their lungs old scars, the evidence of a previous tuberculosis — scars often too small to recognize by the ordinary methods of clinical investigation. Many of us in this room have such changes in our lungs — scars that tell of an old battle fought and won by our organism. It is interesting and sometimes important to know that a man has had such an experience in the past. It is interesting to know that he has such shadows in his lungs, but from the x-ray plate the radiologist can only guess at what those shadows represent. 'Tis for you with your knowledge of the symptoms and the physical signs that you can make out on examination to determine whether such shadows represent the evidence of active disease or the inactive scar that tells of the dead process. The x-ray plate only gives you another bit of purely physical information which can properly be interpreted by careful correlation with all the other elements in the case. Many of these x-ray records revealing, 'though they may, our past experience, are but post-mortem evidence of a process that was, but is no more.

In other instances, a reasonably intelligent consideration of the history of the patient and the nature of the physical signs, should have led the careful examiner to the conclusion that these shadows indicated an unresolved pneumonia or a persistent bronchitis with small areas of broncho-pneumonia of non-tuberculous origin. But these officers had come to rely so blindly upon the x-ray plate with its accompanying and too often unqualified statement "pulmonary tuberculosis," that they had become incapable of observing and properly weighing the physical manifestations which would have justified, in most instances, a correct diagnosis. This blind reliance upon laboratory tests and the associated neglect of the use of one's senses and the ordinary methods of physical examination is sadly common among the profession at large. Not long ago I saw, in consultation, a gentleman who was said by his physician to be suffering from cardiac disease; he feared, angina pectoris. I asked him what the symptoms of the patient had been. His reply was that at first he had thought he had indigestion, but that Dr. X had found his heart enlarged; that Dr. Y had made a Wassermann reaction which was negative; that Dr. Somebody Else had looked into the conditions of the stomach; that a differential blood count had been made; that the urine showed no abnormalities. I asked him if the patient had had pain. He had, over the heart. Did it radiate into any other part of the body? No. Was it associated with exercise? He thought not. After a little questioning I realized that the doctor had practically no information to give me himself as to the symptoms or physical signs of the patient. I then saw the patient and in a few minutes learned that his pains did follow exercise and eating; that they did radiate into his arms in a characteristic manner; that the history alone was such as to justify the diagnosis of angina pectoris. The doctor had neglected all ordinary methods of investigation and had contented himself wholly with the reports of laboratories and experts on this, that or the other detail. This is not to practice medicine, nor is such an individual qualified safely to treat a patient.

The information which the laboratory brings is invaluable to the competent physician, but it can be utilized properly only when weighed in connection with the history and physical examination. The fundamental physical examination that one makes with his eyes, ears and fingers is far more important than any other method of study to which you may appeal. It is inexcusable that a physician today should graduate from a medical school untrained in the basic principles and practice of physical examination; but it would surprise you to know how few officers in the Army—and by that I mean the profession at large—are capable of recognizing the presence of fluid in the chest in any but the simplest cases.

The art of physical diagnosis depends upon observation, experience and judgment, upon what Corvisart has called *"l'education medicale des sens,"* "the medi-

cal education of the senses." It cannot be learned from books. The only way in which you can learn to make a proper diagnosis is by making yourself familiar with the normal by learning to detect deviations from the normal, by working out yourself the significance of those deviations from the normal upon the basis of what you have learned concerning the abnormal changes associated with disease; and this is to be learned only by following your patients from ward to necropsy room.

Deviations from the ordinary or normal make themselves apparent in various ways: by differences in the size and shape of organs, changes which are readily correlated with what you have seen in the anatomical and pathological laboratories; by difference in the rhythm of action or the sounds produced by organs in the performance of their function; by differences in the constitution of body fluids or in the various products of secretion or excretion of organs; by a multitude of modifications of the color, habit, bearing, gait, mentality of the sufferer. You must at first become familiar with the normal and with the manifestations produced by normal organs in function.

In your course on physiology you have learned much about the normal function of most of the vital organs, but there are certain methods of testing and appreciating these functions which are rarely taught in the course of physiology. The student is introduced to these methods ordinarily in the presence of patients showing pathological manifestations. This is, it seems to me, undesirable. It is very common for the student to pass directly from the study, in class room or in laboratory, on lower animals, of the normal anatomy and physiology of the lungs and heart, to the study in the living human being of the symptoms and signs of disease. He is introduced to the various instruments of precision commonly in use, only or almost only, in connection with their application to the detection of disease. A far more rational procedure would be to allow a student, while he is engaged in his physiological studies, to become familiar with the use of methods and instruments of precision as applied to the normal individual, to become familiar, for example, with the movements of the normal chest, with the sensations conveyed by palpitation under normal conditions, with the sounds to be elicited by percussion of the lungs and the abdominal viscera, with the methods of outlining the position and size of the organs, as well as with the sounds which are to be heard on listening to the normal respiration or to the heart's beat. He should become familiar with the phenomena associated with the normal function of heart and lungs as revealed by physical examination, but especially should he be familiar with the physical explanations of these phenomena. If, for instance, you are familiar with the sound of respiration over a normal lung and appreciate the reasons for the existence of such a sound, you will then quickly note any changes from this normal with which you may meet, and you should be able to make rational deductions as to the disturbances of function which may have caused them.

Next year you must be lead through a series of the commoner deviations from the ordinary or normal. If you become familiar with the manifestations of the normal heart in function, if you become familiar with the character of the sounds produced by the normal heart, and with the accepted physical explanations of their cause; and if, later, you come across an individual, in whom, let us say, the second sound of the heart shows peculiar modifications, you will be face to face with an interesting problem concerning which you should be in a position to reason intelligently. The normal second sound is due to certain physical conditions. Here it is modified, perhaps replaced by a new and unusual sound. You will naturally assume that there has been some interference with the normal processes to which the second sound is due, with the closure of certain valves. You will notice on careful examination that this modification of the second sound is heard in certain areas only and, by further consideration, you determine its distribution in relation to the direction of the blood current and the anatomical disposition of the cavities of the heart. And then you will consider the associated modifications of the outline and

size of the heart, and of other sounds, which may indicate that the pressure is raised in cavities behind the valve at which this unusual sound is produced. Further you may find evidences of the engorgement of the venous circulation as shown by the veins of the neck, or enlargement of the liver. There may be modifications in the character of the radial pulse. In the end, by a process of deliberate reasoning, you will arrive at the conclusion that you are perhaps dealing with an insufficiency of a valve, the closure of which is normally associated with the production of this sound, the insufficiency of which might account for the whole train of manifestations that you have observed. Now, when you have once worked out correctly a problem of this sort, as most of us will, if you go into the subject as you should, you will have taken a long step forward, and you will have gained confidence in your own powers of reasoning which will have been used exactly as you will have to use them throughout your life as a practitioner of medicine.

I greatly hope that before many years much of the work you are now beginning may be undertaken in connection with the courses of anatomy and physiology, so that at the same time the student may familiarize himself with the form and functions of the organs in the laboratory and in the living human being.

In the third year, as I have said, you will study selected patients exemplifying changes occurring in the heart and lungs and abdominal viscera. We shall try to give you an opportunity to do this in small groups and in such manner that you may learn to work out your own diagnoses.

To most of the sounds elicited by percussion of normal or diseased organs, to some of the normal sounds or modifications of these sounds arising in heart or lung, in health or in disease, there are applied specific terms, terms introduced for brevity and convenience. Often unfortunately the terms employed to describe a given sound vary somewhat according to the author. He who starts the study of physical diagnosis by reading books on auscultation and percussion finds himself sadly confused when he is confronted by the patient. A safe way, indeed, to confuse yourself and to delay your proper development as an individual capable of detecting disease, is to begin the study of physical diagnosis by reading books, to form pictures in your mind of what these various sounds and manifestations may be and of what they indicate. Such a course places a student at the outset at a disadvantage. It is inconceivable that he should form a correct idea of what he is to hear in the chest from the description that he reads in a book. Fancy that you have never seen or heard a violin, how near do you think you could come to a conception of the sound of a violin from a description read in a book? The parallel is exact. If you begin by reading a book on physical diagnosis you start with a preconceived idea as to the character of the sounds and manifestions with which you are going to meet. This idea cannot be wholly right, and it may be very difficult to rid yourself of it. You will start with a preconceived conception as to the significance of the sound which you have come to associate with the term, which may interfere gravely with the proper use of your reason. You may, before you know it, find yourself reduced to a condition alas, far too common in medicine, that of seeking to make a diagnosis by the matching of a mental picture gained from a description with that which you find before you. The individual to whom diagnosis means matching pictures is lost!

The bane of physical diagnosis, indeed, of medicine in general, is the terminology. Words! Beware of the careless use of words! A word or a term means to many who hear it an instant mental picture. And too often to that mental conception we are forever enslaved. Most of the troubles of mankind are due to the tyranny of words. It is a dangerous thing, thoughtlessly to coin a new word or a new term. Think, only, of the tragic confusion in the minds of men today arising from the term a "League of Nations!"

Of one thing you may be sure: the picture that a given term suggests to another will never be the same as that which it suggests to you. For heaven's sake remember that terms are made for convenience. To paraphrase Seneca, "The term, if thou

knowest how to use it, is thy handmaiden, if thou knowest not, 'tis thy master." Let the term be your handmaiden and not your master. Remember that it is used merely as a convenience; that it is not the essence. Don't allow yourself to think of the manifestations of disease in the sense of a word or a term. Don't let the term itself usurp in your mind the picture that for simplicity's sake it is used to evoke. The reverent attitude of some physicians toward terms comes dangerously near putting them in the category of the good woman who, filled with wonder at the discoveries of the astronomer, begged him to tell her how he had accomplished that which seemed to her the most remarkable of all, the discovery of the names of the stars!

During the next year you should endeavor especially to learn to describe the manifestations of disease in the simplest possible manner, and to use as few unnecessary terms as possible. Be simple and clear in your language and descriptions. If you use a term to describe a sound, for instance, about which there can be doubt in anyone's mind, you are not simplifying, you are confusing; rather describe the sound. And I beg of you, never invent a new term unless it is absolutely necessary.

The safest way to avoid pitfalls is at the beginning to read nothing about physical diagnosis beyond that to which we refer you here. You need no book on physical diagnosis this year. You must work out your own salvation. Nobody can do it for you. Books won't do it for you. Prayer won't bring it to you. On your technical skill and your ability to reason without preconceived ideas, from the information that your senses bring you, on the basis of your physiological, anatomical and pathological learning, depends your success as a physician. If you proceed without books and work out your diagnoses gradually and step-wise through the use of your own gray cortex, you will be following the course that you must pursue during life in dealing with any new or unusual feature of disease. You will not be unduly disturbed by preconceived ideas, and you will not readily forget the explanation or significance of changes which have been detected by your own powers of reasoning.

This year the work will be restricted to the study of the normal individual. But as we study the procedures for the detection of the position of normal organs, the methods of controlling their normal functions; as you study in the healthy individual the movements and sounds to which the normal organs of the chest give rise in the performance of their functions, you will readily appreciate most of the modifications which gross physical changes in those organs should produce, and you will be able to detect and interpret the manifestations of the diseases with which you will meet next year far more quickly than you imagine.

After all, the summary and description of the methods of examining a patient which are to be found in the works of a recent author by the name of Hippocrates, are perhaps as clear and sound as any that have been set forth: "At the outset determine the similarities to, and deviations from, the normal, the most severe, the easiest to recognize, those recognizable in any manner whatever. Look for that which may be seen, felt, heard, which may be appreciated by sight, by touch, by hearing, by the nose, by the tongue and by the powers of reason; in a word all that can be discovered by such powers of appreciation as we possess."

SURGERY

WAR, RAILWAY, INDUSTRIAL, GYNECOLOGICAL, OBSTETRICAL AND UROLOGICAL

ACUTE PANCREATITIS (PANCREATIC NECROSIS) BASED UPON PERSONALLY OBSERVED CASES*

By Joseph Colt Bloodgood,
M.D., F.A.C.S.,
Associate Professor of Clinical Surgery,
Medical Department, Johns Hopkins University,
Baltimore, Md.

This type of pancreatic lesion is less frequently observed than that of chronic pancreatitis and carcinoma.

Although the literature is rich in excellent contributions, the majority of physicians and surgeons frequently neglect to think of acute pancreatitis when confronted with a patient suffering with an acute abdominal lesion, and when the abdomen is opened the surgeon often fails to look for the most characteristic evidence, fat necrosis. And even when he finds this evidence, he is somewhat in a dilemma as to what constitutes the best method of treatment. Two recent cases observed in February and May of 1919 have stimulated me to review again all of my records of cases of this lesion and carefully to go over the notes on my own cases and those in the literature which were very complete up to 1904.

CASE REPORTS

Case I.—Pathol. No. 22012. Acute pancreatitis. Symptoms of ten hours' duration. Operation: drainage of the lesser peritoneal cavity through a mid-line incision and drainage of the gall-bladder. Recovery.

This patient was referred to me by Dr. Talbott, of Baltimore. She was a white female, aged fifty-two, fat and overweight, but her general health was excellent. Some twelve years previously her gall-bladder had been drained and an impacted stone removed from the cystic duct. For more than eleven years she had been free from any attacks of indigestion and of gall-bladder colic from which she had suffered for a number of years before that operation.

During the last three months before the present attack, she had had a return of her old indigestion, but nothing like acute gall-bladder colic.

In these recent attacks of so-called "indigestion" the pain was in the epigastrium on both the right and left side, associated with some belching of gas. Although she consulted a physician, the attacks were so slight that nothing was done beyond the administration of some simple medication.

Present Acute Attack.—Ten hours before admission to St. Agnes Hospital the patient was awakened out of a sound sleep by an intense pain in the epigastrium, present on both sides and somewhat of a girdle character. She immediately vomited the undigested evening meal, which had been eaten without discomfort and with relish some six hours previously. Since then, she had vomited three times a clear, bile-stained material. In those ten hours she had received one and one-half grains of morphine—one-half grain by mouth and the same dose twice hypodermatically. There had been no movement of the bowels. On admission to the Hospital the patient was suffering pain, but less acutely in character. She was positive that it was on both sides of the epigastrium and often went around the entire body below the diaphragm, of a so-called girdle character. At this time, and later during her convalescence, the patient informed me that in all her gall-bladder attacks previous to the operation twelve years previously she felt certain that she had never had an attack similar to that nor suffered so intensely from pain. She also without suggestion volunteered the information that she had never been so prostrate in her old attacks as she was in that one.

Examination.—The patient was not cyanotic, a point emphasized by Halsted. She looked, however, ashy, which might have been due to the large dose of morphine. The pulse was 88, the respirations about 26, chiefly thoracic; the blood pressure 120-80. There was no jaundice. The patient stated that she felt prostrated and nauseated. But she lay quietly on her back with the lower limbs extended. The abdomen showed no marked distention except from fat. The upper halves of the recti muscles were held rigidly and over the epigastrium there was some tenderness. There was no increased sensitiveness in the region of the gall-bladder. The lower recti and lateral abdominal muscles were fairly well relaxed. The area of liver dullness was present and there was no dullness in the flanks.

The temperature per rectum was 100°; leucocytes, 13,600; polymorphonuclears, 71 per cent.; r. b. c., 4,350,000; hemoglobin, 90 per cent. The specific gravity of the urine was 1.030; it was acid and gave no reaction for albumin and sugar.

*Read by title before the American Gastro-Enterological Association, Atlantic City, June, 1919.

Gastric lavage removed a large amount of brown-stained fluid which showed a total acidity of 3; no HCl; bile was present.

We had evidence, therefore, that the contents of the duodenum with bile were regurgitating slightly into the stomach, although it was sixteen hours since any food had been taken and ten hours since the vomiting began. An enema brought away a small amount of bile-stained fecal matter.

Clinical Diagnosis.—I felt quite positive that we were dealing with a pancreatic lesion.

Operative Pathology.—The operation was performed two hours after admission, about twelve hours after the onset of the first pain. The patient took the anesthetic, ether, quietly, and during the operation the pulse rose from 80 to 120 and the blood pressure varied from 120 to 130. The full anesthetic time was one hour and twenty minutes.

Exposure of Gall-Bladder.—I decided that it was wiser to expose the gall-bladder through a right rectus incision for drainage and also to ascertain whether any stones were present. In the thick subcutaneous fat there was no fat necrosis. On opening the peritoneal cavity adherent omentum was encountered. This was apparently huge. In it I could see no fat necrosis and no signs of hemorrhage, but the omentum was infiltrated with serum, having the appearance as if recently injected with salt solution. We could observe in the upper portion of the wound the blue, distended gall-bladder surrounded by this adherent and edematous omentum. The liver above appeared normal in size and color. These omental adhesions were not disturbed. Although it was twelve years since the drainage of this gall-bladder, it was still adherent to the parietal peritoneum.

(It is important to note here that in spite of these adhesions the patient had remained free from any discomfort for a period of more than eleven years.)

When the gall-bladder was opened, the wall was thin and the contents, bile, appeared normal. No stones could be found. Above and to the left of the gall-bladder there was an opening through which I could see the stomach, and this organ was not distended, and when I palpated this area it was not adherent. My finger could pass over the pylorus down over the duodenum to the right. There were no adhesions there.

I felt confident that there was, from the clinical picture, a pancreatitis with fat necrosis. The edema and infiltration of the omentum was to me a new phenomenon, but this was the earliest case that I had had the opportunity to observe or read about.

A tube was sutured into the gall-bladder with chromicized catgut and the right rectus wound was closed with buried catgut and silver wire through-and-through.

Exposure of the Pancreas.—An incision was made in the mid-line above the umbilicus. The subcutaneous fat was not so thick and there were no fat necroses. On opening the peritoneal cavity there escaped a little clear fluid, not the brown-stained peritoneal exudate so characteristic of the later hours or more fulminating form of pancreatitis. The omentum exposed in this area was not adherent, and I could see neither fat necroses nor areas of hemorrhage. The stomach was seen. It was not distended. Bringing the greater curvature of the stomach into view, a point for perforating the omentum and gastrocolic ligament was selected 3 cm. below the stomach in a non-vascular area. After passing through fat at least 4 cm. thick, I exposed and nicked a membrane resembling peritoneum, and then there escaped a blood-stained fluid, but not the characteristic dark-brown fluid already mentioned. The lesser peritoneal cavity had, therefore, been opened. Gently enlarging this opening with retractors and sponging out the fluid, I could feel and see in the depth the pancreas. It was covered by the transparent posterior peritoneal membrane. Its definite markings could be recognized, and the pancreatic tissue, instead of being white, was of a livid pink, and on the peritoneal covering I could see and feel three sulphur-colored granules, so typical of the fat necrosis. The clinical diagnosis was therefore confirmed, and I had seen for the first time the earliest stage of the so-called acute diffuse pancreatitis. The area of pancreas seen was not much larger than that of a silver dollar, while the area palpated was very much larger. But I did not palpate either the head or the tail of the pancreas, as this would only have produced more trauma. Nor did I pull out the omentum and transverse colon in order to inspect and palpate the pancreas through the mesocolon. The colon and small intestines were not seen during the operation. The edema of the omentum was much more marked in the area about the gall-bladder than in the area through which the pancreas was exposed.

I did not make incisions into the pancreas as recommended by von Mikulicz, and followed later in this country by Porter, because in my experience drainage of the lesser peritoneal cavity down through the pancreas had apparently been sufficient.

Drainage Through the Lesser Peritoneal Cavity.—Through the opening I passed a large rubber drainage tube to allow the escape of any fluid and surrounded this by iodoformized strips of gauze in order to isolate, wall off and make a direct fistula between the skin and the lesser peritoneal cavity down to the diseased pancreas. The wound above and below this drainage was closed with silver wire. In both subcutaneous fat wounds two small Carrel rubber tubes were placed in order to facilitate the escape of necrotic fat. If one does not provide for the escape of this material, the entire subcutaneous fat wound is apt to break down, and subsequent events in this case demonstrated the value of this protective drainage.

Post-operative Convalescence.—Twenty-one days after the operation the patient showed every evidence of a complete recovery. When she came out of the anesthesia her first remark was, "You have relieved me of my pain." The tube in the gall-bladder had drained bile and came away spontaneously on the fifteenth day. There was still a slight discharge of bile from this wound. There was some discharge of necrotic fat from the lower angle of this wound.

The drainage from the lesser peritoneal cavity

was of a serous character and slight. The larger tube and gauze had been removed on the twelfth day and two smaller Carrel tubes had been introduced. These tubes were irrigated daily with salt solution. Beginning on about the fourteenth day, the patient had an evening temperature of about 102° and some epigastric discomfort. Two days later when irrigating this wound, there was removed four or five ounces of a white granular material resembling broken-down fat, and then twenty-four hours later more of this material. Since that time there was no fever and no discomfort.

REMARKS ON CASE I

Based upon my own experience and the literature, I have come to the conclusion that this type of drainage of the lesser peritoneal cavity is of the utmost importance. I have not as yet sufficient evidence that this alone is curative in the fulminating fatal type of the so-called acute hemorrhagic pancreatitis. But this form of drainage does relieve the accumulated fluid in the lesser peritoneal cavity and thus relieves tension, and it provides for the later escape of necrotic fat and of necrotic pancreatic tissue. In some of my cases so drained there has been no escape of any material except serum; in other material similar to that in this case, while in still other cases masses of necrotic tissue have come away which, when studied microscopically, showed the connective-tissue framework of the pancreas.

In my own series this is the earliest case subjected to operation, and I have yet to find an earlier one in the literature. It differs from all the other early cases which I have observed or read about in the absence of any bloody or brown exudate in the general peritoneal cavity, and in the absence of fat necroses until the pancreas had been exposed in the lesser peritoneal cavity.

This may be explained either by the fact that in this case the pancreatitis was less acute, or it was exposed to view by an earlier operation. The recovery in this case is no proof that very early intervention will cure all cases of acute pancreatitis of this and the more fulminating type, but it does prove that it provides for proper drainage should the pancreatic necrosis go to the stage of suppuration with the formation of a pancreatic or peripancreatic abscess. My study of the problem seems to show that pancreatic abscess never recovers without operation, and there has been a large mortality in late operations. This evidence should be sufficient to indicate our attitude toward acute pancreatitis when observed and recognized in its early hours.

The problem is: what shall we do in those cases of the fulminating type which rapidly develop the clinical picture of shock in the first twenty-four hours. One group of observers advises immediate operation irrespective of shock; others advise delay, fearing that the additional shock of the operation will lessen the chance of the patient in his or her resistance to this trypsin toxemia. Many years ago, when I first went over this subject, I rather favored the latter view; but on further study of the problem with larger experience, I am inclined to the opinion that immediate operation would increase rather than diminish the chances of recovery.

Up to the present time I have never had an opportunity really to test this view. because the cases in which I have operated recently have not been of the fulminating type.

CASE REPORT

Case II.—Pathol. No. 24143. Acute pancreatitis. Not relieved by removal of stone from, and drainage of, the gall-bladder. Eighteen days later drainage of a peripancreatic cavity filled with cloudy fluid and fat necroses in its wall. Recovery.

This patient was operated upon at St. Agnes Hospital February 7, 1919, by my colleague, Dr. Seegar, who removed a number of soft stones and drained the gall-bladder.

Operative Pathology of First Operation.—Dr. Seegar's notes are as follows: On opening the peritoneal cavity no fluid and no fat necroses were observed. The finding which impressed the surgeon most was a large mass in the region of the pancreas. (The patient was not jaundiced at the time of the operation.) This mass pressed the stomach against the anterior abdominal wall, and the organ was collapsed. The mass felt smooth and was somewhat round or oval in shape. It was present on both sides of the vertebral column; it extended up under the stomach and liver; and it did not pulsate. The right kidney could be palpated and entirely separate from this mass, but the tumor prevented palpation of the left kidney and spleen. It was the size of the head of a fetus. This mass in the region of the pancreas apparently pressed up against the gall-bladder and the cystic duct. (It is important to state here again that the patient was not jaundiced.) The gall-bladder contained a number of soft stones. There is no

note on any adhesions about the gall-bladder. The gall-bladder was drained in the usual way and the wound closed.

Clinical History Previous to First Operation.—The patient was a white female aged 37. She was overweight and very fat. Acute attacks simulating indigestion and gall-bladder colic had taken place at irregular intervals for the past five years, and in some of these attacks there had been jaundice. Between the attacks the patient was apparently in good health. There was usually vomiting during the attacks and the pain radiated to the shoulder.

During the past eight months the attacks had been more severe, of longer duration, and her family physician informed Dr. Seegar that as a rule in these later attacks the patient had been collapsed. The symptoms had at times been so serious that in his opinion myocarditis was present.

The patient entered St. Agnes at the end of a very severe attack in which there was marked collapse in the early hours. Under observation in the Hospital the patient would have an attack of pain, vomit, and the pulse would become very weak,—so much so that on one or two occasions there seemed to be every evidence that she would not recover. It was for this reason that the operation was delayed. Pancreatitis, however, was not considered, but some myocardial lesion. The examination revealed nothing but a mass in the umbilical and lower epigastric area and tenderness and muscle spasm in the region of the gall-bladder. The urine contained no sugar.

When operated upon February 7 by Dr. Seegar, the patient took the anesthetic well and was not shocked.

Post-operative Notes After First Operation.—In spite of drainage of the gall-bladder, the patient was not relieved of her epigastric discomfort and intermittent attacks of pain, during which the pulse would become very weak. At my examination I could palpate a deep mass between the lower left costal margin and the umbilicus, and this mass was sensitive and the seat of her pain. Palpation on the right side was prevented by the wound. There was no jaundice.

Second Operation, February 25, 1919.—At this time the tube in the gall-bladder had been removed, but the sinus was still discharging clear bile. It was eighteen days since the first operation. The patient took the anesthetic well. The average pulse was 100; blood pressure, 130. The incision was made in the mid-line, above the umbilicus. There was no fat necrosis in the very thick subcutaneous fat, nor in the preperitoneal fat. On opening the peritoneum there was no fluid, but a few disseminated fat necroses could be seen on the surface of the omentum. The omentum was not adherent in this area, nor were there hemorrhages or edema. Lifting out the omentum and transverse colon, I could feel and see an indurated pancreas through the mesocolon extending to its tail. I could also feel a mass apparently on top and surrounding the pancreas, bulging anteriorly above the mesocolon and extending up behind the stomach. The mass was evidently smaller than when Dr. Seegar operated eighteen days previously.

The omentum and colon were replaced in the peritoneal cavity and an opening in the omentum was made in a manner similar to that described in Case I. On making this opening numerous fat necroses were seen. Deep down in this area I could see and feel a tense membrane, but on this membrane I saw no fat necroses as in Case I. On nicking this membrane, there escaped at least a pint of cloudy fluid containing white granular material (probably necrotic fat tissue). This material resembled that which escaped from the drainage sinus in Case I on the fourteenth day. This fluid was sponged out. The fluid seemed to occupy the lesser peritoneal cavity. What felt like the pancreas, formed its posterior wall. It extended toward the tail in greater depth than toward the head of the pancreas. It extended upward behind the stomach, and it was limited downward by the mesocolon.

It is very interesting to note that the fluid from this cavity which escaped on the exposed tissue produced an almost immediate reaction, so that the tissues stuck together as if they had just been covered with some adhesive substance.

The drainage of the cavity and the closure of the wound were similar to Case I.

Post-operative Notes After Second Operation. The patient had no further attacks of acute pain, nor of collapse with a weak pulse. She volunteered almost immediately the information that she was much more comfortable than after the first operation. Nevertheless, the convalescence to complete recovery was much slower than in Case I. There was discomfort in the epigastrium and tenderness in the region of the tail of the pancreas for at least one month. The sinus discharged more purulent material and some pieces of what appeared to be necrotic pancreas. But this tissue was not preserved for microscopic examination. The patient did not leave the Hospital for two months.

REMARKS ON CASE II

It is quite possible that this is the type of pancreatitis which later, if not operated upon, develops into a peripancreatic cyst and may become of huge dimensions.

SUMMARY OF PERSONALLY OBSERVED CASES

I find that I have notes upon nine additional cases, making a total of eleven cases between the years 1894 and 1919, a period of twenty-five years. This may be looked upon as evidence that the majority of surgeons have a relatively small experience in the diagnosis and operative treatment of this type of pancreatic lesion.

In reviewing these records, I wish to investigate the following questions:

1. Can pancreatitis be diagnosed clinically?

2. Should operation be performed immediately, even in those fulminating cases first seen in a condition of extreme shock or collapse?

3. What is the best method of exploring the pancreas and of treatment when evidence of acute pancreatitis is found?

CASE REPORT

Case III.—Pathol. No. 513. Acute pancreatitis. Abscess. Operation. Recovery.

I assisted Dr. Finney in this operation in 1894. The case was diagnosed clinically by Dr. Thayer and reported by him in the *American Journal of Medical Sciences* in October, 1895. In this instance nothing was done but drainage of the abscess. The gall-bladder and ducts were not exposed at the operation. The patient was well in 1913, nineteen years after operation.

Clinical History.—The patient is a white male aged 34, overweight and fat, with a history of excess of alcohol, both beer and whiskey. For two years he suffered with morning nausea and intermittent attacks of epigastric pain and vomiting, but no jaundice.

He was admitted to Johns Hopkins Hospital on the tenth day of his first very acute attack, which consisted of epigastric pain, vomiting,

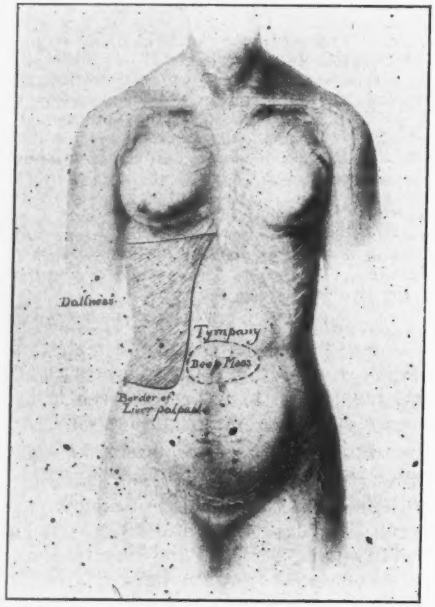

Fig. 1, Case III. Pathol. No. 513. Acute pancreatitis, abscess, tenth day of attack. To illustrate the position of the palpable mass and the enlarged liver.

fever, distinct toxic delirium, and the examination revealed a mass above the umbilicus. (See Fig. 1). There was no jaundice. The clinical feature which impressed me most was the evidence of toxemia and delirium. The palpable mass was distinctly in the pancreatic area. The liver was enlarged.

Operative Pathology.—An incision was made in the mid-line above the umbilicus. The liver was enlarged, the stomach adherent to the liver and below the stomach a mass of fat tissue (omentum) studded with yellow, sulphur-like granules (fat necroses). A mass could be felt deep below this omentum behind the stomach, and apparently in the lesser peritoneal cavity. At this time we were not familiar with the fact that pancreatic abscesses are sterile. It was the first case ever observed in the Hospital, and for this reason gauze was packed into the peritoneal cavity between the omentum and the parietal peritoneum.

This operation had no effect upon the fever nor delirium. It relieved the vomiting but not the nausea. A loop of small intestine was coughed out of the wound on the fifth day, and I replaced this with additional gauze drains. On the seventh day Dr. Halsted explored with his finger the exposed omentum studded with fat necroses and opened a large cavity filled with purulent and necrotic tissue. The patient's general condition rapidly improved. During convalescence a number of large pieces of necrotic tissue were discharged from the sinus. These were examined microscopically and showed areas of fat necrosis and the typical stroma of the pancreas. The patient left the Hospital at the end of three months with a small sinus, which healed in a few weeks.

Although this abscess was operated upon on the tenth day, it was really not drained until the seventeenth day, and there is no question that a portion of the pancreas sloughed and was discharged from the wound.

We have no evidence in this case that in the beginning of the attack there was any collapse, nor that it was the fulminating type of pancreatitis. However, the symptoms in the first twenty-four hours were sufficiently characteristic to allow a diagnosis. The later symptoms were fever, delirium and tumor, undoubtedly due to the necrosis of the pancreas and the peripancreatic abscess.

Case IV.—Surgical No. 10574. Acute pancreatitis. Abscess. Operation under local anesthesia (Bloodgood) on the twenty-first day of the acute attack. Death twenty-four hours after operation.

This case has been reported by me in the *Johns Hopkins Hospital Bulletin* for January, 1901. The autopsy was reported by Opie in the *American Journal of Medical Sciences* for January, 1901. The autopsy in this case demonstrated a stone in the diverticulum of Vater similar to a case reported by Halsted and autopsy reported by Opie. But in Halsted's case there was no abscess.

Clinical Note.—The patient was white, male, aged 47. He was not overweight; there was no excess of fat; and there was no history of alcohol. For a number of years there had been attacks called "indigestion." Seven months before admission to Johns Hopkins Hospital there was a severe attack of pain and jaundice lasting three weeks. This was diagnosed gall-stones.

The patient was admitted to the medical side of Johns Hopkins Hospital on the eighteenth day of his last attack. In this attack the onset of

pain had been more intense than in the previous attack seven months previously. During the first twenty-four hours there was vomiting, but none since then. On the third day there was fever, and on the seventh day a distinct mass in the epigastrium.

Examination.—This was very similar to that of Case III. The patient showed delirium and slight jaundice. The leucocytes were 19,000 and the boggy mass (Fig. 2) which could be palpated. The liver was not enlarged as in Case III. The patient was observed on the medical service three days.

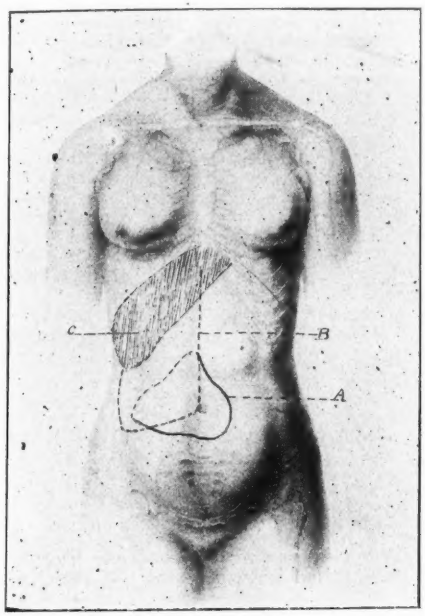

Fig. 2, Case IV. Surg. No. 10574. Acute pancreatitis, abscess; acute symptoms 21 days. A—palpable tumor; B—visible distention; C—liver dullness.

When I saw him with Dr. Futcher I made the diagnosis of pancreatic abscess because of my distinct recollection of Case III.

Operation.—Upon opening the peritoneal cavity the omentum presented itself studded with fat necroses and distinctly edematous. The omentum was adherent by fresh adhesions to the parietal peritoneum. There was no difficulty, by blunt dissection with the finger, in making a hole in the omentum and exposing a second mass covered with fat and fat necroses. This mass was aspirated, and in so doing there were withdrawn a few drops of blood. By blunt dissection, after passing through 3 cm. of fat matted together with an inflammatory exudate and studded with fat necroses, I evacuated a liquid material. The first that flowed out was yellow and gelatinous, and the next brown and thick, like chocolate. The cavity was apparently a large one and had numerous pockets. Cover-slips and cultures showed a bacillus which was not thoroughly worked out.

Autopsy.—The abscess was well drained and there was no peritonitis. The pancreas was very necrotic, and there was a small stone in the diverticulum of Vater.

REMARKS ON CASE IV

Why did this patient, whose abscess was drained on the twenty-first day, die, and the patient in Case III, whose abscess was drained on the seventeenth day, recover? My notes show that the condition of the patient in Case IV was much more critical. The temperature was 104°, the pulse 130, and the respirations, 40.

The diagnosis in this case could have been made in the first few hours of the attack, and most certainly on the seventh day, when a mass could be felt. There is every reason to conclude that an immediate operation would have resulted in recovery.

Case V.—Pathol. No. 8256. Acute pancreatitis, apparently subsiding. Operation on the fifth day. Recovery.

Clinical Note.—This patient came under my observation at St. Agnes Hospital, in 1907. Up 'till that time I had observed pancreatitis only twice, both abscesses (Case III, in 1894, and Case IV, in 1900) and I was naturally gratified that I made the diagnosis in this case on the fifth day.

The patient was a white male aged 43. He was slightly overweight and fat. There was no history of alcohol. It is very important to note that there was no history of previous attacks nor of infectious diseases nor of trauma.

Before retiring one night feeling well, he drank two glasses of cold milk and ate a large amount of chocolate candy. Three hours later he was awakened with intense epigastric pain and vomiting. The pain was so intense that he sent for Dr. Kempter, of Chambersburg, Pa., who gave him morphine hypodermatically, and observed him very carefully. At the end of sixteen hours slight jaundice and high colored urine were observed. The vomiting had ceased, the temperature had risen to 102°; the pain was confined to the epigastrium; and there was distinct rigidity of both upper recti muscles. Dr. Kempter gave the patient no more morphine and nothing by mouth but water. The pain and fever gradually subsided and the jaundice disappeared.

I saw the patient at St. Agnes Hospital at the end of three and one-half days.

Examination.—The pulse varied from 90 to 100, the temperature from 100 to 101°. The patient states that he still has some epigastric discomfort, and in this area there is distinct tenderness and some rigidity. The liver dullness is present and not enlarged; the respirations

are abdominal,26; no mass can be felt, and there is no area of abnormal dullness in the abdomen. The leucocytes were 13,000 with a slight increase in the polymorphonuclears. Although the patient is not restless he looks ill. There is no jaundice and the urine does not give the reaction for bile. The bowels moved by enema. Any food (he was given only liquids) increases the epigastric discomfort.

Diagnosis.—This patient was observed one and one-half days, and my notes made at that time (May, 1907) on the first case of this kind which I had observed read as follows:

The clinical picture suggests acute pancreatitis with recovery, but the possibility of a developing abscess should be considered, and in view of the fact that there are still residual symptoms, it seems the wiser plan to operate.

Operative Pathology.—Although I felt that it was pancreatitis, I first explored the appendix through a small incision at the outer border of the right rectus. On opening the peritoneal cavity there was no fluid, and out of this wound there protruded a small piece of omentum studded with fat necroses. A second incision was made in the mid-line above the umbilicus. There was no fluid; a few fat necroses were found in the omentum, but no hemorrhage and no edema. The stomach, transverse colon and small intestines were not distended. The pancreas was exposed as already described in Cases I and II. As I approached the pancreas the fat necroses increased in number. There was no fluid in the lesser peritoneal cavity. I was not able to see the pancreas as described in Case I, and on palpation the pancreas did not feel abnormal. The gall-bladder was not distended and contained no stones. The drainage in this case consisted of gauze and rubber tissue.

Post-operative Notes.—The patient claimed that he felt relieved of his epigastric discomfort. There was no discharge, except the serous fluid that one observes after drainage in the peritoneal cavity.

The drains were removed on the thirteenth day and the patient left the Hospital at the end of four weeks with a very small sinus, which healed rapidly.

Ultimate Result.—In 1916, nine years after operation, the patient wrote that he had had no further attacks and that he was well.

REMARKS ON CASE V

Apparently this was the type of acute pancreatitis which recovers, and it is a question in this case whether operation had anything to do with the recovery. Apparently in this case and in Case III there was no relation to gall-stones. If there were any necrosis of the pancreas in this Case V, it must have been absorbed, because no necrotic tissue was discharged through the sinus.

Case VI.—Pathol. No. 8936. Acute pancreatitis with cholecystitis and gall-stones. Operation three days after onset. Death twenty hours after operation associated with complete anuria.

Clinical History.—This patient was referred to me at St. Agnes in 1908 by Drs. Mahale and Holiday. She was critically ill and the examination at once suggested either the fulminating type of acute pancreatitis or general septic peritonitis.

The patient was a white female, aged 45, unmarried. The extreme cyanosis noted by Halsted was present. The pupils were pin-point, probably due to morphine. The respirations were entirely thoracic and gasping. The pulse was very weak and rapid. The leucocyte count was 40,000, the temperature 100°. The abdomen was very much distended, the muscles very rigid, the patient wincing whenever a muscle was pressed upon. On percussion, tympany; no areas of dullness. On catheterizing the bladder there was very little urine. At the end of the third day from the beginning of the attack she was thus described by me, and the critical symptoms have been observed less than twenty-four hours. For the first two days of the attack, according to the physician, the pain was chiefly in the right lower quadrant, and it was looked upon as a slight attack of appendicitis.

The patient was too ill to give any information direct, and both physicians were positive that for two days there had been no very severe symptoms, and that the bowels had moved after enemas until twenty-four hours previously. If that history were correct, it rather suggested a perforated appendix with a general streptococcic peritonitis. The patient was also profoundly under the influence of morphine. There had been no vomiting of fecal character.

Operative Pathology.—The area of the appendix was explored through the outer border of the right rectus. On opening the peritoneal cavity there was no fluid and no signs of peritonitis. The appendix was normal, although the small intestines were quite distended with gas. On the omentum seen in this exploration there were no fat necroses as noted in Case V. The pelvic organs were normal. On pushing the cecum to the medial side some cloudy fluid was observed which apparently was flowing from the region of the gall-bladder. I then made an upper right rectus incision. The gall-bladder was distended and tense; there were no adhesions; in the space between the gall-bladder, liver, duodenum and meso-transverse colon, there was a serous cloudy fluid. On sponging out this fluid I saw in the mesentery of the transverse colon fat necroses. This is shown in Fig. 3. Apparently this is an unusual place. The pancreas was enlarged. There was no evidence of hemorrhage into the tissues. As the gall-bladder contained stones and very dark bile, the stones were removed and the gall-bladder drained. I also drained the space between the colon, duodenum and gall-bladder, where we found the fluid and majority of fat necroses.

As the patient was critically ill, I had to work very rapidly, but it is my opinion now that it would have been better had I drained the lesser peritoneal cavity through an incision in the gastrocolic omentum as described in Cases I and II.

Sir Berkeley Moynihan, of Leeds, England, was present at this operation, and said that he had seen similar fat necroses in exploring the gall-bladder.

The patient rallied well from the shock of the operation. A rectal tube brought away gas and fecal matter, but catheterization of the bladder found but 30 c. c. of urine.

Previous History in Case VI.—Later I ascertained from the family of the patient and her physicians that for five years she had suffered with intermittent attacks of abdominal pain and vomiting, and that some months previously she had had a very acute attack in which she was prostrated, and that two weeks before her last attack she had been confined to bed for two days.

It was ascertained, also later, that five days before she came into St. Agnes Hospital the patient had had an attack of acute diarrhea, and that in the present attack noted as of three days' duration, the very acute symptoms began forty-eight hours instead of twenty-four hours before her admission to the Hospital.

This retaking of the history demonstrates how difficult it is to get the exact facts and the exact duration of the acute attack. This element of error adds to the difficulty when we try from the study of a number of cases to come to any definite conclusions. But apparently in this case the patient had suffered from sufficiently characteristic attacks to indicate operation some years earlier, and certainly, in this present attack the intervention could have been earlier, before her condition had become critical.

Fig. 3, Case VI. Pathol. No. 8936. Sketch of operative findings showing area of fat necrosis on mesocolon between gall-bladder and duodenum; gall-stones in the cystic duct; adhesions between cystic duct and duodenum.

REMARKS ON CASE VI

This clinical picture corresponds with that form of acute pancreatitis described as fulminating, in which the patient is in shock or collapse. There is a difference of opinion as to whether or not operation should be done. Personally, I have no evidence that anything is to be gained by delay, but as far as I can make out from my own cases and those in the literature, the chief hope of relief depends upon the recognition of the condition before shock, or collapse takes place, and in the majority of cases this seems possible. In Case I, reported in this paper, twelve or twenty-four hours' delay may have found this patient in a condition of collapse.

Case VII.—Pathol. No. 9900. Acute pancreatitis with definite cyst in the lesser peritoneal cavity and cholecystitis with gall-stones. Operation was done in 1909. Drainage of the cyst in the lesser peritoneal cavity and of the gall-bladder through two incisions. Recovery. Postoperativve complication, peripheral neuritis.

Clinical Note.—I was reminded of this case during my operation in Case II, as they were very similar in clinical history and operative findings.

I operated upon this patient in Hagerstown in August, 1909, for Dr. Wertz, and I made the correct clinical diagnosis based upon my previous experience with two cases of pancreatic abscess (Cases III and IV) and a third case operated upon by Dr. Mitchel, in Washington, tissues

from which were sent to me with the record.

This patient (Case VII) was a female, aged forty-five; slightly over-weight and with excessive fat. For a number of years there had been intermittent attacks of indigestion without jaundice. The present attack had been more severe and of longer duration than any previous attack. The patient had been ill for at least six weeks. Very quickly after the onset of pain and vomiting there was jaundice and epigastric tumor. The jaundice had disappeared and the tumor had become smaller (compare with Case II). But the patient continued to have epigastric distress, and nausea and vomiting when she took much food. On account of this the diet had been so restricted that she had lost fifty pounds. Despite this she was still over-weight and fat.

This was similar to the clinical picture in Mitchel's case, in which a clinical diagnosis of cancer of the stomach with pyloric obstruction was made.

Examination.—On inspection nothing abnormal was detected about the abdomen. On palpation a deep mass (Fig. 4) was felt in the middle of

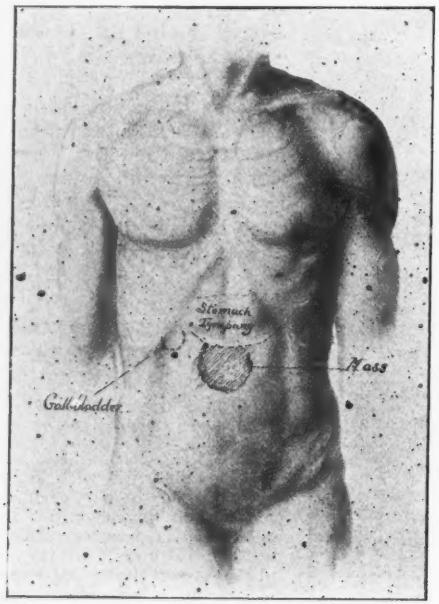

Fig. 4, Case VII. Pathol. No. 9900. Acute pancreatitis with cyst in lesser peritoneal cavity and cholecystitis with gall-stones. Sketch to show the position of the palpable mass and palpable gall-bladder.

the epigastrium above the umbilicus, very much as in Fig. 1. The mass was round, the size of two fists. It did not move with respiration. It could be moved from right to left. There was distinct pulsation, which seemed to be transmitted as if the mass rested upon the abdominal aorta. There was not the expansile pulsation of an aneurism. The hand could be placed between the ribs and the mass on both sides. The tumor appeared too suddenly for either a new growth or an aneurism. It followed a distinct attack of gall-bladder colic. As the stomach was empty and there was no muscle spasm, it could be palpated most satisfactorily.

Operative Pathology.—An upper right rectus incision was made. On opening the peritoneal cavity no fluid was found. No fat necroses were present in the omentum. The tumor could immediately be palpated (Fig. 5) through the omentum,

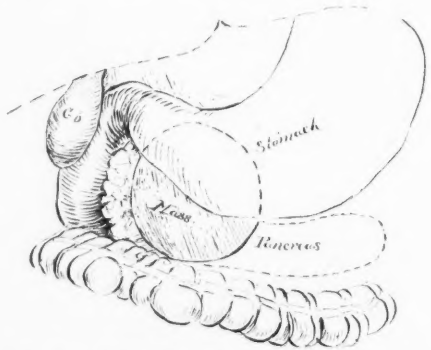

Fig. 5, Case VII. Pathol. No. 9900. Sketch to demonstrate the relation of the cyst in the lesser peritoneal cavity to the stomach and colon. The great omentum has been omitted from the sketch.

and behind the stomach, which was not distended. The stomach was pushed forward and upward, as in Case II. The tumor bulged between the stomach and the transverse colon. On removing the omentum and transverse colon I could easily outline the tumor through the mesocolon. I could palpate the tail of the pancreas to the left of the mass and the head of the pancreas to the right, and could demonstrate that the left loin was not the proper place through which to drain this cyst or chronic abscess in the lesser peritoneal cavity. The gall-bladder was filled with stones, but its walls were not thick and it was not distended. The tumor was then exposed through the omentum and gastrocolic ligament, as described in Cases I and II, but through this incision and not through a separate mid-laparotomy. Up to this time no fat necroses had been observed. But in going through this fat I found a few areas of fat necrosis, but these were distinctly different in color from those observed in the more acute stage of pancreatitis, being a very pale yellow and of more crystalline appearance. On passing through the gastrocolic omentum I exposed a distinct cyst wall, elicited fluctuation, excluded expansile pulsation, and on aspiration obtained clear fluid. On incising this cyst there was first a clear fluid, and then distinct chocolate colored fluid containing globules of fat (see Case IV). This material was not present in Cases II and III. The cyst contained about five ounces of this material. As soon as we had sponged out the fluid the cyst col-

lapsed. I could not see the pancreas, nor did palpation demonstrate that it was very much indurated. The cavity was drained with a tube and iodoformized gauze similar to Cases I and II. The gall-bladder was opened, emptied and drained with a tube. The bile was black and viscid. A stone was also removed from the cystic duct which was at first overlooked.

The closure of this wound with two distinct drainage tubes surrounded by gauze was complicated, and I am confident that for drainage of the lesser peritoneal cavity the mid-line incision, as described in Cases I and II, is preferable.

Postoperative Notes.—I saw this patient again on the ninth day. The gall-bladder tube was draining well, but the drainage of the lesser peritoneal cavity was not satisfactory. For two days there had been vomiting and fever with rapid pulse. I removed the drainage and washed out from the cavity purulent material, necrotic fat and what appeared to be necrotic pancreatic tissue. This gave almost immediate relief.

One month later the patient was admitted to St. Agnes Hospital with the definite clinical picture of multiple neuritis associated with a mental syndrome. The diagnosis was confirmed by my associate, Dr. Herring. These symptoms began about the fourteenth day. As far as I can make out the healing of the drained cavity did about as well as in Cases I, II and III in this paper. It is the only case of multiple peripheral neuritis that I have observed after operation. The patient was very slow in getting well and has never fully recovered. But she has had no further attacks suggestive of gall-stone or pancreatitis, and no sugar in the urine.

Case VIII.—Pathol. No. 9856. Apparently a case of recurrent acute pancreatitis associated with chronic pancreatitis. First operation was cholecystostomy. (No jaundice at that time.) Second operation was drainage of the common duct. (Jaundice at that time and fat necroses were found at operation.)

Clinical Note.—This patient was referred to me by Dr. Futcher, at Johns Hopkins Hospital, in 1909. He was a white male, aged 61, of apparently good health, slightly overweight and very fond of good living, with a moderate amount of alcohol. For a number of years this patient had suffered with intermittent attacks of epigastric colic and glycosuria. Apparently each attack was definitely associated with overindulgence in food and alcohol. He was admitted to the Johns Hopkins Hospital at the end of the third week of a rather severe attack from which he had not completely recovered. There had been jaundice in that attack which had practically disappeared. The examination revealed sensitiveness and muscle spasm in the region of the gall-bladder. There was neither fever nor leucocytosis. The clinical picture was one of cholecystitis, and a definite relation of the attacks to food, and the intermittent glycosuria suggested also a chronic pancreatitis.

Operative Pathology.—On opening the peritoneal cavity no fluid and no fat necroses were seen in a very large omentum. The gall-bladder was distended, the walls thick, and the omentum and mesocolon were adherent to the gall-bladder. The latter contained no stones, but a great deal of white gelatinous material, which microscopically proved to be hypertrophied Luschka's glands. The cystic, command and hepatic ducts were distinctly thickened by an inflammatory reaction, which was also present in the wall of the duodenum, and the pancreas as far as it could be palpated was indurated. But I could find no fat necroses. We had, therefore, a definite picture of an inflammatory process involving the head of the pancreas, the duodenum slightly, and the gall-bladder and ducts. This condition must have been subsiding, because the jaundice at operation had disappeared and the fever which had been present in the early days of the attack had subsided.

Drainage of the gall-bladder completely relieved the patient's symptoms. The sugar had disappeared from the urine before operation.

Second Attack.—I warned this patient against any overindulgence in food or alcohol. He was readmitted to the Johns Hopkins Hospital September 28, about two months after the first operation. For the first month after operation he was free from attacks, but then he returned to hard work, and on three occasions broke his diet at banquets, which occasions were immediately followed by definite attacks. The first, one month previously, consisted of a sharp attack of epigastric pain lasting for two hours. The second attack, two weeks previously, was characterized by more pain, fever and jaundice, lasting a few days. The third attack, one week before readmission, was most severe in epigastric pain, in chills with temperature rising to 103°, and with definite jaundice. The patient was observed for two days. Although the skin was still jaundiced, bile had returned in the stool and had almost disappeared from the urine. Although the temperature did not rise above 100.5°, the leucocytes remained at 22,000.

Operative Pathology at Second Operation.—No fluid was found in the peritoneal cavity. More adhesions were seen than at first operation, which were easily separated, bringing into view the gall-bladder, which was not much distended, the cystic duct, the common duct, which was greatly distended (not distended at the first operation), and the pancreas, which was much more indurated than at the first operation. Over the head of the pancreas there were distinct disseminated fat necroses. On opening the common duct there were no stones. A probe could easily be passed into the duodenum. Both the common duct and the gall-bladder were drained.

Result.—This patient recovered and had no further attacks up to 1917, eight years later.

Because we did not find fat necroses at the first operation is no evidence that they were not present in the lesser peritoneal cavity. There is no question that they were present at the second operation. One might conclude from a case of this kind that drainage of the common duct is more effective in this type of pancreatitis with obstuction to the common duct, than drainage of the gall-bladder. There is apparently no question that at the first operation we observed a distinct pathological picture of cholangitis and cholecystitis associated with pancreatitis, but the inflammatory lesion was subsiding, and there also ap-

pears to be no question that at the second operation the chief lesion was a pancreatitis, but that the swelling of the head of the pancreas which had blocked the common duct was subsiding.

Case IX.—Pathol. No. 14039. Acute pancreatitis. Clinically and at operation diagnosed intestinal obstruction due to cancer or diverticulitis of the sigmoid. This patient died six days after operation (colostomy of the cecum) and an autopsy demonstrated a necrotic pancreas with fat necroses.

Clinical Note.—I saw this patient with Dr. Cassidy on April 14, 1913, twenty-four hours after the onset of what the patient and his family insisted was the first attack; and after a most careful history and examination made an incorrect diagnosis and operated four hours later and did not recognize, on opening the abdomen, the lesion that had produced the symptoms. In this case surgical history repeated itself, because in the majority of cases of acute pancreatitis the diagnosis of intestinal obstruction had been made.

This patient was a white male, aged 62. Before this attack his health had always been good. However, he was overweight, very fat, of sedentary habits and a huge eater; but he did not use alcohol to excess. This first attack began a few hours after eating peanuts and ham sandwiches. There was first intense abdominal pain in the epigastrium. The patient then took a number of doses of cathartics, which increased the pain, but did not produce vomiting nor a stool. When seen by Dr. Cassidy, in about the eighth hour of the attack, he was suffering intensely with pain in the epigastrium, but Dr. Cassidy found no muscle spasm. Morphine gave temporary relief of pain, but the patient again took cathartics without instructions from his physician, which not only increased the pain, but produced vomiting. This was twelve hours after the beginning of the symptoms, and for the next twelve hours pain and vomiting were characteristic symptoms.

Examination.—Twenty-four hours after the onset the patient was vomiting bile-stained material. He looked slightly cyanotic and toxic. The temperature was 104°; the respirations (thoracic) were 30; and the pulse 100. The patient had just taken an enema, and during the examination had a sudden abdominal colic different from the epigastric pain, which was quickly followed by a foul-smelling, liquid stool. The examination at St. Agnes Hospital, about two hours later, found the leucocytes to be 23.000. Gastric lavage brought away bile-stained fluid. An enema was ineffectual. The cyanotic and toxic appearance had increased; the distention was more marked; all the abdominal muscles were slightly rigid; the liver dullness was not obliterated, and there was no dullness in the flanks.

Diagnosis.—My notes state that we considered chiefly sigmoiditis with partial obstruction, and decided to explore in the region of the cecum for a temporary colostomy. As I review this case, I remember distinctly that I did not think of pancreatitis, and I cannot conceive now why I did not make a diagnosis of pancreatitis. The symptoms were far too acute and developed too rapidly to be associated with obstruction of the colon.

Operative Pathology.—On opening the peritoneal cavity cloudy fluid was encountered. Had the fluid been blood-stained or brown, I should have at once suspected pancreatitis. But this fluid is not always present, especially in early cases. On the omentum there were no fat necroses, which were fortunately present in the omentum in Case V. But experience has led us to know that we cannot always depend upon finding fat necroses, especially in early cases, outside of the lesser peritoneal cavity. The small intestines were more distended than the large. This should have made me suspicious of my diagnosis of obstruction of the sigmoid. When I explored the sigmoid from the right wound, I got the impression that its surrounding fat was indurated. But every surgeon knows the difficulty of diagnosis by palpation, when the patient has a huge omentum, fat appendices epiploicae, and large amounts of fat in the mesocolon. The appendix was removed and the cecum was sutured to the parietal peritoneum for later opening.

Postoperative Notes.—The symptoms were not relieved. There were hiccup and vomiting of fecal character, not relieved by gastric lavage. Thirty-six hours after operation the cecum was opened, and this was followed by the discharge of huge quantities of fecal material. Following this there was great improvement in the general and abdominal condition of the patient. Vomiting ceased; the hiccup, however, although better, persisted. The distention almost disappeared.

For two days the patient was apparently improving. Then there was a sudden change for the worse: hiccup without vomiting (lavage showed no gastric retention), diminished urine, delirium and rapid pulse. Death.

Autopsy.—A partial autopsy was made by the resident, Dr. Loos, who found fat necroses in the omentum between the stomach and colon, hemorrhages, bloody fluid in the lesser peritoneal cavity; a huge pancreas covered with fat necroses, and containing areas of pancreatic necroses. There were no gall-stones (there had been no jaundice). The microscopic examination of the tissue removed confirmed the diagnosis of fat necroses and areas of necrosis in the pancreas.

REMARKS ON CASE IX

In view of this patient's condition at the time of the operation, twenty-eight hours after the onset of the attack, and the number of days that he lived after the operation (six days), I am inclined to the opinion that if the correct diagnosis had been made and the lesser peritoneal cavity drained, as in Cases I and II, the patient would have recovered.

The evidence of obstruction of the colon as revealed at the operation was not sufficient. I should have explored the upper abdomen through a second incision.

Case X.—Pathol. No. 18229. Acute pancreatitis with cholecystitis and gall-stones in the gall-bladder. Operation seven days after the begin-

ning of the attack and twenty-four hours after the beginning of the symptoms with collapse. Drainage of the lesser peritoneal cavity and gall-bladder. Recovery.

Clinical Note.—This case cannot be considered one of fulminating pancreatitis, but the patient was critically ill and was getting worse. I made the correct diagnosis in this case.

The patient was a white male, aged fifty, admitted to Johns Hopkins Hospital September 15, 1915. The suggestive etiological factors were typhoid fever eleven years previously for the gall-stones; overweight, obesity and overindulgence in food for the pancreatitis. There were definite previous attacks—first, for a few years of belching after meals; then, for eighteen months, attacks of epigastric pain and belching beginning two hours after meals and disappearing five hours after eating. Often in these attacks the patient would induce vomiting to relieve the pain. The attacks were at first once a month; then twice a month. Seven months previously there was a very acute attack with jaundice lasting five days. These attacks all suggest gall-stones.

The present attack began seven days ago. At the onset the pain was so intense that he showed signs of collapse. The most marked feature has been that anything taken by mouth not only gave discomfort, but was as a rule not retained. If the patient took no food nor water, he had less discomfort and no vomiting. Despite an almost starvation diet, the patient had a second attack of intense pain with collapse twenty-four hours before admission, and jaundice appeared for the first time.

Examination.—The patient complained chiefly of pain in the epigastrium, more marked on the left side, but the intensity of the pain had abated. Even small quantities of water produced vomiting. The vomitus was bile-stained. The jaundice was disappearing, and enemas brought away brown fecal matter. The pulse varied from 100 to 116; blood pressure, 126; respirations, 24; and the leucocytes were 22,000. The abdomen was moderately distended in the upper half; the upper halves of the recti muscles were rigid; sensitiveness was slight. The patient looked toxic, but there was no cyanosis.

The most marked symptoms were regurgitation of any food, muscle rigidity, and pain in the epigastrium.

Operative Pathology.—A diagnosis of pancreatitis and gall-stones was made. A right rectus incision to explore the gall-bladder revealed brown-stained fluid in the peritoneal cavity. A distended, thick-walled gall-bladder contained stones. In separating adhesions between the gall-bladder and duodenum fat necroses were found in the fat over the head of the pancreas and in the parietal peritoneum. A second incision was made in the mid-line above the umbilicus. There were fat necroses in the omentum. On opening the lesser peritoneal cavity through the gastrocolic omentum there was evacuated a brownish fluid which microscopically contained blood and chemically bile and pancreatic ferments. The pancreas was not seen, but was felt to be enlarged and indurated. The lesser peritoneal cavity was drained as noted in Case I; the stones were removed; and the gall-bladder was drained. The closure of the wound was similar to Cases I and II. It is interesting to note that the staphylococcus albus was found in the fluid from the gall-bladder, but the fluid in the lesser peritoneal cavity was sterile.

Post-operative Notes.—The patient remained in the Hospital forty-one days. For some days epigastric discomfort and hiccup persisted. From the lesser peritoneal cavity there was discharge not only of purulent material, but of pieces of necrotic pancreatic tissue.

The subcutaneous fat in both wounds became necrotic, but the silver wire sutures through-and-through prevented the gaping of the wound. For at least fifteen days the drainage from the gall-bladder and the lesser peritoneal cavity were not perfect, but after that time drainage was apparently perfectly established and the patient's discomfort disappeared and his general condition improved.

Ultimate Result.—It is now (June, 1919) almost four years since the operation, the patient is well and has suffered from no recurrent attacks.

Case XI.—Pathol. No. 20724. Acute pancreatitis with jaundice; one stone in the gall-bladder. Operation forty-eight hours after the onset of acute symptoms. Drainage of the lesser peritoneal cavity and gall-bladder. Recovery.

Clinical Note.—This patient was referred by Dr. Slade, of Reisterstown, Md., on December 19, 1916, forty-eight hours after the beginning of an acute attack. The diagnosis of acute pancreatitis was made and operation performed at once.

The patient was a white female, aged forty; overweight and obese. In 1908, eight years previously, I had operated upon her for chronic lactation mastitis, but at that time we were not suspicious of any gall-bladder lesion. The patient, however, had then suffered from attacks of indigestion, but had paid no attention to them. Four months before operation she was admitted to St. Agnes Hospital under the care of my colleague, Dr. Freeman, who made the diagnosis of chronic cholecystitis and advised operation, which was refused. At that time the patient was suffering with intermittent attacks of epigastric pain and vomiting, especially after the morning meal.

The attack which preceded the operation was more acute than any previous attack. There was intense pain in the epigastrium and in the gall-bladder area. The pain was referred to the shoulder. Vomiting of all food; jaundice.

Examination.—Temperature, 101°; leucocytes, 16,000; and blood pressure, 144. The pulse varied from 68 to 102. Slight jaundice, but some bile in stools. Definite distention in the epigastrium, muscle spasm and sensitiveness with definite tenderness and muscle spasm in the gall-bladder area.

Operative Pathology.—A right rectus incision for exploration of the gall-bladder. Clear fluid was found in the peritoneal cavity. A few fat necroses were seen on the omentum. The gall-

bladder was not distended. There were adhesions. One stone was present in the gall-bladder; no stone in the duct. The head of the pancreas was indurated. A second incision was made in the mid-line. Fat necroses were seen in the omentum. On opening the lesser peritoneal cavity there escaped blood-stained fluid and more fat necroses were found in that region. The pancreas was not seen, but felt very much indurated. Drainage as in Cases I and II.

Post-operative Notes.—Rather rapid recovery. No discharge of necrotic pancreatic tissue from the lesser peritoneal cavity. June, 1916, the patient was two and one-half years well.

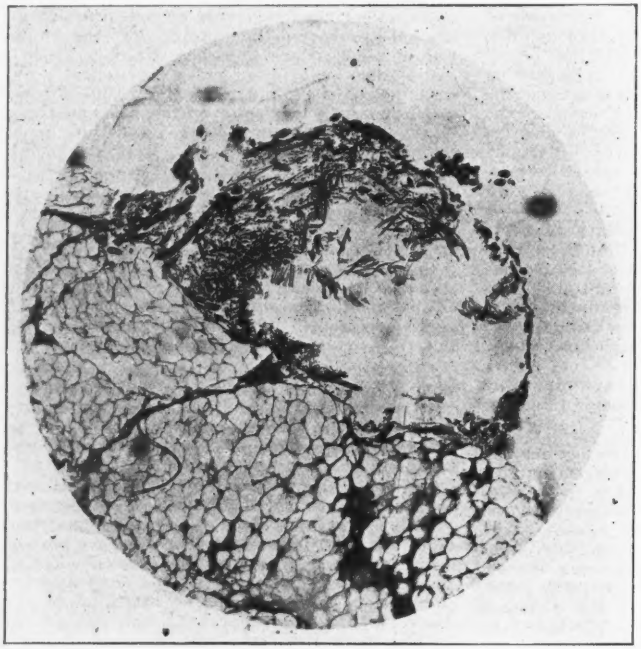

Fig. 6, Case XI. Pathol. No. 20724. Photomicrograph (low power) of area of fat necrosis in omentum.

Microscopic Appearance of Fat Necroses.—From this, Case XI, I removed a small area of fat necrosis and Fig. 6 illustrates the microscopic appearance.

CONCLUSIONS

Can pancreatitis be diagnosed clinically? Yes. The characteristic symptom is pain in the epigastrium present on both sides. If there is vomiting, the pain is not relieved by it. The most suggestive sign on examination is the sensitiveness in the epigastrium and the rigidity of the upper portion of both recti.

When the patient is carefully questioned, he will admit a distinct feeling of prostration all out of proportion to the duration of the pain and rarely, if ever, observed in an equally severe pain of the gall-bladder or kidney.

The signs of prostration may not be evident in the pulse rate and blood pressure. Fever and leucocytosis appear to be late symptoms.

PREVIOUS ATTACKS

In the majority of cases there will be a history of previous attacks of one or two types: epigastric pain and distinct gall-bladder colic. When the latter is present, gall-stones or cholecystitis are found at operation.

A history of jaundice in previous attacks, or evidence of jaundice at the examination, can not be looked upon as characteristic of pancreatitis, nor do they exclude pancreatitis.

The great majority of these patients show not only overweight, but various degrees of obesity. They are all of sedentary habits, and with hardly an exception are overeaters. Overindulgence in alcohol is distinctly a factor of less importance than overindulgence in food.

CLINICAL DIAGNOSIS

This is essential, because the evidence of pancreatitis may not be found until the lesser peritoneal cavity is opened. (See Case I.)

RELATION TO GALL-STONES AND CHOLECYSTITIS

In the literature this relationship is rather overemphasized. The majority of surgeons—perhaps all—will operate upon from 100 to 300 cases of gall-stones or cholecystitis and meet only one case of acute pancreatitis in which drainage of

the lesser peritoneal cavity is essential for recovery.

There seems no doubt that there is a definite relationship between pancreatitis and gall-stones, with or without cholecystitis, and cholangitis, and Opie's explanation of regurgitation of bile may explain some but not all the cases. Apparently we have not as yet exact knowledge as to the etiological factor or factors, and we must for the present attempt to make the diagnosis and relieve the condition without this exact knowledge of the etiology.

THE CORRECT ATTITUDE OF THE FAMILY AND PHYSICIAN IN THE PRESENCE OF ACUTE ABDOMINAL SYMPTOMS

The public should be instructed that when there is an acute attack of abdominal pain with or without nausea, the best treatment is absolute rest in bed and nothing by mouth, either solid or liquid, and that a physician should be sent for at once.

Both the public and the medical profession should be repeatedly warned against the administration of any cathartic in the early stages of an acute abdominal attack. Ochsner has correctly stated this matter. If a cathartic is needed, no harm will ensue by its delay; if it is not needed, it is dangerous.

Even in this small list of cases, the patient most critically ill had been given huge doses of cathartics, while the patients in better condition had had no cathartics and no food.

MORPHINE

These patients are in such pain that morphine must be given for their relief, but in my experience an abdominal colic not relieved by one hypodermic of morphine should be regarded with suspicion of a lesion requiring immediate operation, and the patient should be at once transported to a hospital, so that an operation can be done at once, if further examination indicates it.

In acute abdominal lesions enemata and gastric lavage are helpful in making the patient more comfortable, in preparing them for operation, should it follow, and are often of diagnostic value.

The careful examination of these patients in the first few hours of the attack, and the obtaining of a correct history from the patient or family, should in the majority of cases lead to a correct diagnosis, at least to the point of sending the patient to the hospital, where one with larger experience will be able to make the diagnosis as to whether operation is indicated or not, and this patient will be in far better condition not only from the fact of earlier intervention, but because the acute lesion has not been irritated by cathartics or food, or obscured by an overdose of morphine.

DIET

As the vast majority of patients who come under observation in the critical stage of acute pancreatitis have been warned by previous attacks, the public and the general profession should be instructed on the importance of paying more attention to vague symptoms of indigestion and to slight attacks of epigastric pain and belching or vomiting, with or without a transient jaundice, and the most important treatment is not drugs, but restriction of diet, a most thorough examination, and, if possible, an operation before the acute attack takes place.

It is quite possible that pancreatitis without accompanying gall-stones can be relieved by proper diet and reduction of overweight and obesity.

I know of no definite finding in a thorough examination which will allow a diagnosis of pancreatitis unless the patient is seen in an attack of epigastric pain and rigidity. The diagnosis must be made more by exclusion and from the history of the attacks.

SHOULD OPERATION BE PERFORMED IMMEDIATELY, EVEN IN THE FULMINATING CASES FIRST SEEN IN A CONDITION OF EXTREME SHOCK OR COLLAPSE?

The evidence strongly suggests that death in acute pancreatitis, with or without abscess, is due to a toxemia produced by the pancreatic ferments which in some as yet unexplained way gain entrance to the lymphatic or blood circulation. There is no question about the death and the

autopsy findings. Apparently there is no question that recovery takes place in animals in which pancreatitis has been produced experimentally and in the human being with all the clinical evidence of the disease. From my own experience and the reading of the literature I am impressed with the conclusion that drainage of the lesser peritoneal cavity through the gastrocolic omentum meets the indications more than any other suggested treatment.

At this operation the gall-bladder with rare exceptions should be explored and drained if indicated. Perhaps we may learn that in jaundiced cases the common duct should be drained.

My own experience leads me to conclude that the so-called fulminating type of pancreatitis is not common, and that our failures to cure have been due to an improper operation in the early cases or to late intervention. My Case VI is an example of an incomplete operation in a relatively early case, and in Case IX the death of the patient was undoubtedly due to an incorrect diagnosis, while Cases I, X and XI seem to show the efficacy of a correct diagnosis, correct treatment of acute pancreatitis in the early stage.

We must repeat here that preoperative diagnosis is essential. Exploratory laparotomy does not always reveal the blood-stained peritoneal exudate and the fat necroses. Even the exploration of the head of the pancreas when the area of the gall-bladder is explored may not disclose a pancreatitis. The best method of examining the pancreas, if one does not wish to go through the gastrocolic omentum and fat without more evident signs, is to withdraw the omentum and colon and inspect and palpate the pancreas through the mesocolon.

WHAT IS THE BEST METHOD OF EXPLORING THE PANCREAS AND OF TREATMENT WHEN THERE IS DISTINCT CLINICAL EVIDENCE OF PANCREATITIS, OR SIGNS AT THE EXPLORATORY LAPAROTOMY?

This question has already been answered in the preceding discussion.

STRICTURE AND CALCULUS OF THE URETER FROM THE DIAGNOSTIC VIEWPOINT

By Guy L. Hunner, M.D., F.A.C.S.,
Associate in Clinical Gynecology, Medical Department, Johns Hopkins University,
Baltimore, Md.

Those who have had the rare good fortune to follow Sir William Osler in his dispensary and bedside clinics must remember vividly with what enthusiasm he advised the investigation, trial and use of the newer instruments of precision as aids to diagnostic work. Nor do they forget his ofttime warning that we should not become slaves to the modern factory-made helps in diagnosis at the expense and dwarfing of our God-given five senses and powers of ratiocination.

No field in medicine offers more problems in diagnosis than that of the abdominal cavity and Dr. Osler's pupils remember with what zest he tackled the difficulties presented by an abdominal tumor or those suggested by an obscure abdominal pain.

It has long been recognized that stone in the upper urinary tract may give rise to signs and symptoms which make it necessary to consider every other abdominal organ in arriving at a diagnosis. Israel, in 1893, warned us that the first essential in arriving at a diagnosis of stone in the upper urinary tract is to divest the mind of the usual text-book picture of that condition.

Only within the last four years have we begun to appreciate that ureteral stricture may give rise to precisely the same symptoms and signs as ureteral or renal calculus, and that stricture and its sequelæ must, therefore, be considered in attempting to diagnose the cause of obscure abdominal pain.

In the study of about 500 cases of ureteral stricture occurring in my practice in the past four years, I have arrived at a number of important conclusions. Some of these are startling because of their newness, but none of them would be presented here had I not full confidence that time and further investigation on the part

of other men will give them support and verification.

Ureteral stricture is one of the commonest causes of abdominal symptoms in women. Unrecognized ureteral stricture leads to more needless and fruitless abdominal operations than any other pathologic condition. These operations in the probable order of frequency are for appendicitis, ovarian disease, uterine and pelvic disorders, floating kidney, especially the type with hydronephrosis, gall-bladder investigations, and abdominal explorations for intestinal obstruction and adhesions.

In addition to the operations, we have prolonged treatments and rest cures for gastrointestinal and other abdominal symptoms, treatments for sacral joint troubles and for sciatica.

On the other hand, in dealing with a disease that has such protean symptoms as to call for such a variety of useless treatments, and particularly in dealing with a condition that occurs so frequently, if we are not constantly on our guard, we may persist in treating a ureteral stricture after the symptoms due to it have subsided and neglect to remove a diseased appendix or gall-stones which are crying out for attention. In particular, we are liable to neglect a spinal arthritis or sacral joint disease, for these may come from the same focal infection that caused the stricture.

Ureteral stricture is the cause of more kidney pathology (excluding conditions usually classified as medical) than any one factor. It accounts for the majority of hydronephrosis cases, and thus indirectly for many cases of floating or movable kidney and of pyonephrosis. The majority of pyelitis cases have ureteral stricture and obstruction as a basis. Most cases of pyelitis of pregnancy and of the puerperium depend upon stricture, as do many cases of pyelitis in children. Some cases of albuminuria and eclampsia leading to premature childbirth are due to stricture. Most cases of stone in the ureter and probably many cases of stone found in the kidney and bladder arise in an area of ureteral stricture. It is probable that urinary stasis due to stricture is the predisposing factor in many cases of stone arising in the kidney and of recurring kidney stone after operation. Many, if not the majority of the cases of so-called essential or idiopathic hematuria are due to ureteral stricture.

Finally, time and experience have amply verified my original theory that most cases of ureteral stricture and many cases of chronic urethritis are due to focal infections.[1]

In this paper we are to deal with only one small section of this wide subject, namely, the differential diagnosis between ureteral stricture and ureteral calculus.

The chief value of such a discussion lies in convincing the profession that the diagnosis can not be made without special urological methods, and that operation is not justifiable until these methods have been employed in an effort to arrive at a correct diagnosis.

There are usually exceptions to dogmatic statements and one may admit at once that in certain cases with symptoms typical of stone in the ureter one can easily palpate the stone through the vaginal or rectal route, or more rarely, in thin patients, a stone may be palpated in the abdominal portion of the ureter. One can never be certain in such cases, however, that he is not palpating a venous phlebolith in the lower pelvis or a calcified lumbar gland in a patient whose symptoms of renal colic are due not to this condition, but to ureteral stricture.

How often the cock-sure and, alas, even the modest surgeon, spends an uncomfortable hour or two sweating in the search for the ureteral stone that is not present. Every surgeon with experience knows how difficult it is at times to locate a stone when present, and he will agree that it is not fair to subject the patient to the ordeal of a serious operation in making a differential diagnosis between ureteral stricture and stone when far simpler means are at hand.

One may admit also that there are rare instances in which life may be jeopardized by the delay necessary for special examinations. In the case of a patient with a past history of renal colic, who is suddenly taken with a fresh attack and is going into coma, it might be our duty to make the diagnosis and relieve the situation by immediate operation. This

would be particularly true in the case of a young or middle-aged patient seen under circumstances that would not justify the delay in having an x-ray photograph, or an examination with the renal catheter.

If we admit the identity of signs and symptoms in patients suffering with stricture or stone, it becomes apparent that we must use special urological methods for a complete diagnosis.

We are indeed fortunate in having developed methods which have converted an intricate field of surgical diagnosis into one of the most accurate and scientific branches of the medical art.

While I am an enthusiast over the use of the cystoscope, the renal catheter and the roentgen ray, and believe that no surgeon is justified in operating upon questionable lesions of the upper urinary tract without first giving the patient the advantages of the use of these three methods of diagnostic precision, I wish, before illustrating some of the points to be gained by their use, to emphasize first the importance in all urinary surgery of the older methods of diagnosis.

Scientific surgery of the urinary tract demands first of all a careful anamnesis, physical examination, and urinalysis. I never expect to reach the point in my surgical work in which I shall be satisfied to operate without the knowledge to be gained by the supremely important first-hand information to be obtained from these older methods.

For the benefit of the modern hospital interne and resident who is prone to grumble over his one to five years of history-taking and urinalysis, it may be of service to know that the few contributions I have made to the advancement of urology have all been founded upon the persistent following of this old-fashioned road of drudgery and attention to the minute details of each individual patient.

It may be profitable to summarize briefly the usual routine followed in arriving at a diagnosis between ureteral stricture and calculus.

ANAMNESIS

The chief point to bear in mind is that from the history alone one can not differentiate between ureteral stricture and calculus. Given the typical history with which we have been taught to associate the diagnosis of ureteral stone, and without further data it is about as safe to make a diagnosis of stricture as of calculus, because stricture is by far the more common disease.

The renal colic, the pain down the ureteral line, the bladder frequency or even tenesmus, the rectal tenesmus, the gastro-intestinal symptoms of nausea and vomiting, meteorism, stasis, and the various referred pains in the back, sacrum, rectum, urethra, perineum, hip, and down the leg—all these symptoms, so frequently found with ureteral calculus, are about as often associated with ureteral stricture.

It must be remembered that either a stricture or a stone may be present for years without causing renal colic. In either condition there may be only a mild discomfort which the patient distinctly states can not be dignified as a pain. This discomfort or soreness may be localized at the site of the disease or it may spread to the kidney region. It may be constant or intermittent, occurring at intervals of hours, days, weeks, or months. On the other hand, stone or stricture may be present without local soreness or pain except when the renal colic occurs, and this may be only at long intervals.

The temperature in patients suffering with renal colic due to stricture or stone may be altered much, little, or not at all. Chills may occur with the colic due to stone or stricture. Elevation of temperature may be present only at the time of the colic, or it may be present with the more or less dull, steady pain and soreness and last for days. I have seen temperatures of 103 to 104° due to obstruction from stricture without the presence of infection, but do not recall having seen a case with chills in either stone or stricture obstruction in the absence of infection.

If a patient gives a history of having passed a ureteral stone but still has a continuance of reawakening of symptoms characteristic of stone, we must always think of the persistence of a ureteral stricture in which the stone was formed.

If a patient has passed a stone from one ureter and later complains of symptoms suggestive of stone on the opposite

side, the probable diagnosis is stricture, although of course a stone may be found in this stricture.

PHYSICAL EXAMINATION

In our effort to differentiate the two conditions, the local examination of the urinary tract by means of bimanual palpation may be negative, or it may result in positive findings which are helpful, or which may be misleading and which, if not corrected by further studies, may result in useless operations.

It is rare in either stone or stricture cases that bimanual examination is negative. If the kidney can be palpated it is usually found more sensitive than normal. If infection or hydronephrosis be present, or if there has been a recent attack of colic, the kidney is more sensitive than usual and may be distinctly enlarged.

Palpation of the ureteral area beside the sacral promontory, where the ureter crosses the pelvic brim, nearly always elicits pain, and the patient may complain of a referred pain up toward the kidney, and more often down toward the bladder with a desire to void.

If the stone or stricture be located in the upper pelvis in the region of the bifurcation of the internal iliac artery, the point of maximal tenderness is likely to be found on palpating just below the pelvic brim. These pain phenomena on the right side often lead to the diagnosis of appendicitis. Most strictures and most ureteral stones in women are found in the broad ligament region. Bimanual palpation through the vaginal vault in line with the ureter most often elicits the point of maximal tenderness, and the pain is not infrequently referred up toward the kidney, upward and outward toward the appendix or the sigmoid, outward and back into the hips or sciatica region, or downward into the thigh. At times palpation of the diseased lower ureter brings on rectal pressure, and nearly always the desire to void. The trigonal region of the bladder is not infrequently implicated in the inflammatory process about the broad ligament region, and this will cause palpation of the bladder base to be painful. Patients with disease of the lower ureter, particularly if the trigonum is involved, often complain of dyspareunia, and it is this symptom, together with the above phenomena obtained on palpation of the broad ligament region, that leads to the diagnosis of "ovarian disease," or "pelvic inflammatory disease," and results in needless operations.

The periureteritis associated with stricture or stone can often be palpated as a wire-like thickening in line with the vesical and broad ligament portion of the ureter; at times the local thickening about a stricture in the broad ligament region may be so gross as to feel like a stone, and if further studies are not made, the patient is submitted to a futile operation in the quest for stone.

Another fertile source of error when depending solely upon the history, urinalysis and palpation findings is to mistake a phlebolith in the broad ligament region for a ureteral stone. This will be referred to later under the x-ray findings. Suffice it here to state that the same focal infection that has settled in the lymphatics of the broad ligament may probably cause an inflammation in the ureteral wall, followed by stricture, and an inflammation in the veins, followed by one or more phleboliths. Another finding on palpation, which may be helpful or harmful according to the completeness of our accessory studies, is the discovery of a stone in the region of the abdominal portion of the ureter. Cabot[2] has shown us that such a stone may be a calcified tuberculous lumbar gland.

URINALYSIS

It goes without saying that in discussing urinalysis in women we always mean the examination of a specimen obtained from the bladder by catheterization.

The urinalysis does not help in differentiating between stricture and calculus disease of the ureter. Furthermore, the urinalysis may prove positively harmful to the patient, as it has often done in the past, when the finding of a normal urine has diverted the diagnostician from further investigation of the urinary tract and has led to some useless operation upon some unoffending organ. If the patient is more fortunate, he, or she, is merely labeled a neurasthenic and set aside for rest cures; or rebelling at these, and justly

feeling that legitimate medical science has failed, seeks relief in some of the numerous cults always ready to readjust a dislocated vertebra, or to convince the suffering one that pain is a figment of mortal mind and to be treated as such.

The above dogmatic statements on the value of the urinalysis are intended to emphasize the necessity of more accurate observations in this field. Too often on seeing a macroscopically clear urine the laboratory worker is hurried and careless in his microscopic work and makes a negative report, whereas a more careful analysis would show an occasional erythrocyte or leucocyte to indicate trouble somewhere in the urinary tract.

A patient with stricture or stone may show normal urine during the quiescent stage, whereas an examination during or just after a renal colic is very likely to reveal leucocytes or erythrocytes, or both.

Formerly, we were taught that calculus in the upper tract always caused blood in at least microscopic quantity.[3] More recent observations of long series of cases of ureteral stone show that blood may be absent in from 14 per cent. in 150 cases reported by Cabot[4] to 20 per cent. in 294 cases reported by Braasch and Moore.[5] In my second series of 50 cases of ureteral stricture[6] there were 39 cases without urinary infection, and urine catheterized from the bladder in 36 of these cases showed erythrocytes in 5 cases, leucocytes in 2 cases, and both red and white cells in 3 cases. Twenty-six cases, or 75 per cent., showed normal urine. With the presence of a ureteral stone in a stricture area we are more likely to have ulceration and therefore blood. It is thus seen that the first dogmatic statement made above concerning the value of urinalysis in a differential diagnosis may be modified to the extent of saying that the presence of blood favors the diagnosis of stone. This is especially true if the case be in the quiescent non-painful stage. During the stage of colic the ureteral stricture case may show as much blood as the case of stone.

Recently I have had a number of cases with severe hematuria apparently due to stricture and am confident that this fact is going to throw light upon many cases of so-called essential or idiopathic hematuria. It is probable that the hemorrhage in most of these cases comes from an ulcer in the stricture area, while in others it may come from injury to the kidney due to the back pressure. In some of these cases of hematuria associated with stricture there are no symptoms; in others, there is pain.

A few leucocytes may be found in the urine in the presence either of stricture or stone.

When a stricture or a stone is associated with infection we rarely find a pure bacilluria, but usually a bacilluria with pyuria, and with these some erythrocytes are often present. In cases of complete obstruction of the affected side either from stone or stricture there may be temporary absence of abnormal elements in the bladder urine.

Albumin may occur with stricture or stone and may be dependent upon or, independent of, the presence of blood. In one case an albuminuria of long standing and severe grade and not associated with blood disappeared after dilatation of the bilateral stricture.

From the above analysis it will be seen that our older methods of diagnosis should lead us to suspect stricture or stone in the urine in the majority of patients suffering with these diseases.

The limits of this paper do not permit the classification and discussion of the other lesions of the urinary tract or of the diseases of other organs that have too often been diagnosed and treated in error when these ureteral lesions should have been found and the patient relieved. The author has elsewhere made a fairly complete classification of such diseases.

Our failures in the past have not been due entirely to the limitations of the older methods of diagnosis, and I think we shall all confess that there has been hurried, faulty and careless use of the methods of anamnesis, physical examination and urinalysis.

Our analysis shows, however, that with the most careful use of these methods we get no further in most cases than to state that the symptoms and physical findings point to a lesion of the urinary tract. To locate this lesion, to analyze its character, and to outline its best form of treatment, we are absolutely dependent in most cases

upon the newer methods of urological diagnosis. These in the order of their simplicity and freedom from annoyance to the patient are: roentgenography, cystoscopy, and catheterization of the ureter with its various accessory methods of investigation, such as the bilateral functional test of the kidneys, the use of the wax-tip, wax-bulb, and other instruments for locating and treating obstructions, and the use of shadowgraph materials combined with roentgenography.

Our recent medical literature is so replete with new and ingenious methods of urinary tract diagnosis that I shall not attempt their complete classification, but shall confine this paper to a report on the methods I find useful in my rather limited field of work on women.

ROENTGENOGRAPHY

A positive x-ray picture of a stone in the ureter is of great value for diagnosis when a patient complains of symptoms and reveals signs pointing to a lesion in the urinary tract. A negative x-ray means nothing, but often proves worse than useless, because it stops further investigation of the urinary tract.

Omitting my first 50 cases of ureteral stricture occurring in my first 13 years of practice in which stone in the urinary tract was present ten times, and considering about 500 cases of stricture diagnosed in the past three and a half years, since November, 1915, stone in the urinary tract has been found in approximately 35 cases.

We thus see a tremendous margin of error if we depend upon the unassisted roentgenogram to decide whether the symptoms are due to a urinary tract lesion. Add to this the admission of the expert roentgenologists that they miss from 15 to 30 per cent. of ureteral stones. Consider also the point made when speaking of the physical examination that the symptoms may be due to stricture while the x-ray may show phleboilths or calcified tuberculous glands in the ureteral region.

A patient may be suffering with symptoms due to stricture and the x-ray reveal a stone in the kidney or bladder. As shown in previous publications,[7] such a stone may have originated in the stricture and subsequently floated upward to the kidney; or it may have been forced downward into the bladder. The importance of this observation is apparent to those surgeons who have removed a stone from the kidney only to be disappointed in having the patient continue with his original symptoms which subsequent x-rays fail to explain.

Cabot[8] has called attention to the importance of having the roentgenograph taken at the proper angle to reveal ureteral stone lying in the upper pelvis just anterior to the sacro-iliac joint.

CYSTOSCOPY

The cystoscopic findings may or may not be helpful. Fenwick and others have shown meatoscopic pictures of the edematous reddened ureteral orifice region supposed to be diagnostic of ureteral calculus. In my experience the only cystoscopic picture diagnostic of ureteral stone is to see the stone just within the distended open orifice or partially extruding through the meatus.

The reddening, or reddening and edema, about the orifice, or these signs together with a slight polypoid projection near the orifice, are proof merely of an inflammatory condition in this region, and may be due to trigonitis or to some ureteral lesion, be it tuberculosis, stone, stricture or some other cause of ureteritis. Tuberculosis may be present in the upper tract, or stricture or stone may exist very near the ureteral orifice without the slightest meatoscopic change observable through the cystoscope.

On the other hand, many cases of stricture in the broad ligament region show decided changes about the orifice as do many of the cases with low-lying stone.

In a few cases of ureteral stricture in the broad ligament region the inflammatory process seems to involve the entire region of the base of the bladder or at least that portion of the bladder occupied by the trigonum.

I have a group of ureteral stricture cases in which the chief symptoms have been referred to the bladder, and in which cystoscopy revealed an edematous, reddened trigonum. The ureteral mons region may or may not be particularly edematous and prominent.

These patients have all had bilateral stricture and the history of great vesical distress, and the palpatior and cystoscopic findings would seem to indicate an inflammatory process involving the base of the bladder and both broad ligament regions. The urine may be quite normal or contain leucocytes and erythrocytes.

The cystoscope may be of great value in ureteral diagnosis by demonstrating purulent or bloody urine coming from one or both ureteral orifices. Through the Kelly cystoscope the urine may be caught directly from the separate orifices for macroscopic and microscopic examination. We determine the presence of an abnormal number of ureteral orifices by the cystoscopic examination and may be able to estimate which section of a double kidney is diseased.

We conclude from the above that cystoscopy *per se* often gives us no clue in making a diagnosis of ureteral disease and it seldom helps us in differentiating between stricture and stone in the ureter, but the finding by cystoscopy of a trigonitis or of a reddened ureteral orifice region should make us think of the possibility of ureteral disease.

CATHETERIZATION

The court of last resort in making a diagnosis between ureteral stricture and ureteral calculus is the renal catheter. The catheter unaided does not render a positive decision except in the rare case in which one can feel the grating of a stone as the catheter is introduced or withdrawn. In such cases one is led to examine the gum elastic material carefully and can see scratch marks on the catheter, which confirms the evidence gained through the grating sensation imparted by the catheter.

We must usually depend upon tipping the catheter with wax or upon using a shadowgraph catheter and the x-ray. Even these accessory helps will fail us in many cases unless the catheter is equipped with a wax bulb in addition to the wax tip. The wax bulb is well nigh indispensable in making a diagnosis of stricture and, as we have seen, the vast majority of the cases under discussion are stricture and not stone cases.

The unaided catheter may go to the kidney in either stone or stricture cases without appreciable obstruction. The wax-tipped catheter may go to the kidney with or without appreciable obstruction in the ureter and come back with scratch marks due to a kidney stone, while the patient's symptoms may all be due to ureteral stricture. The wax-tipped catheter may be permanently obstructed in the ureter by a stricture area surrounding a stone, and come back without scratch marks, because the lower end of the stricture is too dense to allow the wax tip to come in contact with the stone.

Any catheter may be obstructed permanently in a broad ligament stricture and yet the patient may still have a higher stricture area with or without a stone.

In case of permanent obstruction to the plain or wax-tipped catheter it is well at the next examination to use the duck-bill open-end shadowgraph catheter and to get an x-ray picture while distending the upper tract with a shadowgraph fluid. This will usually show a dilated ureter above the point of obstruction, whether this is due to stricture or stone; and in case a stone is present, the shadowgraph fluid will often make it visible even when a previous plain x-ray plate has been negative.

If an open-end shadowgraph catheter is obstructed in the broad ligament region and the attempt to inject shadowgraph fluid results in severe ureteral pain after a few drops or possibly one or two cubic centimeters of the fluid has entered the ureter, we should suspect a second stone or stricture obstruction just above the first obstruction, and usually at the iliac gland region. An x-ray view of such a condition may show a stone shadow in the broad ligament region and another longer shadow just above, due to the distending fluid in the ureteral segment between the two obstructions. This second shadow should not be mistaken for a second stone.

The ideal preparation of a catheter for testing in a case of suspected stone or stricture is to make the spiral wax tip and then to place small wax rings at every fifth centimeter on the portion of the catheter that will enter the ureter. The second ring 10 cm. back of the tip should

be made large, between 3.65 and 4 mm. in diameter, and of spindle shape with long, sloping shoulders. If a stone be present its approximate location below the kidney can be read on the wax rings. If the symptoms have been due to stricture or stone, the large wax bulb will have a decided hang on its withdrawal, and by grasping the catheter at the external urethral orifice with the thumb and finger and then drawing the bulb through the obstruction area and out, one can measure from the proximal shoulder of the wax bulb to the thumb and finger and find the distance of the obstruction above the external urethral orifice. Allowing 5 cm. for the urethra and trigonum, one arrives at the location of the lesion above the bladder.

The use of the wax-tipped catheter to determine whether a given x-ray shadow is cast by an intra-ureteral calculus is much simpler in females with the Kelly endoscope than in males, or for those who use the Nitze type of cystoscope for work on both sexes. Harris[9 10] and others have devised means for the use of the waxed catheter through the Nitze type of cystoscope. Fortunately, we may arrive at the same differential diagnosis through the use of the x-ray with the previous introduction of the ureteral catheter with retained metal stylet or with the shadowgraph fluid, or of the shadowgraph catheter or sound.[11]

Even with these accessory methods of diagnosis there is opportunity for error. If the skiagraph catheter and the stone shadow are quite separate we know we are dealing with an extra-ureteral body, but if the two shadows are in juxtaposition or apparently superimposed, we dare not decide the diagnosis until we have used the wax-tipped catheter or obtained another x-ray picture at a different angle or have taken a stereoscopic view.[12]

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THE SIGNIFICANCE OF UROGENITAL DISORDERS IN THE GENERAL DIAGNOSTIC STUDY OF WOMEN*

By Edw. H. Richardson, M.D., F.A.C.S.,
Associate in Clinical Gynecology, Medical Department, Johns Hopkins University,
Baltimore, Md.

A survey of present-day tendencies in medical education, in hospital organization and in the therapeutic application of medicine and surgery, clearly indicates that we have entered upon a new clinical era in the history of our profession. Scarcely more than a decade ago few of our medical schools could boast of as many as a half-dozen clinical professors; a medical student must needs traverse the maze of the entire curriculum to gain the coveted doctor's degree; hospital construction and organization provided adequately for only several of the greater clinical subdivisions, and the value to the patient of efficient co-ordination of even these had not been discoverably appreciated. But what a change has been wrought within a dozen years! Under certain wise restrictions and through the aid of judicious counsel, the medical student may now reach his goal over any one of a number of elective routes; the policies of governing boards, both in the matter of faculty additions and the business of material hospital equipment, are subject to and deserve stricture where they fail to embody the progressive spirit of the times and to supply the demand for new clinical units as the ever-multiplying need of such be-

*From the Gynecological Department of the Johns Hopkins University and Hospital.

comes apparent. And just as the ancient and honorable custom of consultations between practitioners of approximately equal rank and training became largely supplanted in our centers of population, at least, by a growing demand for the more efficient services of the consultant specialist, men of wider experience and superior skill in a limited field, so, in turn, we are now witnessing another interesting and significant change in the method of clinical adaptation. The multiplication and development of medical and surgical specialties have progressed with such amazing rapidity and the resulting contributions to scientific knowledge have reached such staggering proportions that even the greatest minds among us find themselves hopelessly unable to grasp and comprehend them all.

We are confronted, therefore, with the interesting fact that none of us is competent any longer to give the best professional advice to an individual patient, except within a relatively narrow clinical domain. Such designations as "general surgeon," "general internist" or "general diagnostician" are today misnomers, for no such individuals exist, if we mean by these phrases one equally competent in all subdivisions of surgery or internal medicine, as the case may be. These changed conditions have inaugurated a new clinical era in that they already are being met by the profession in an altogether intelligent and satisfactory manner by the substitution of multiple for simple consultations. It is becoming generally recognized now, both by the laity and the profession, that in all maladies of an obscure or even serious nature the services not of one or two but of a coterie of highly trained specialists are required, if the individual patient is to obtain the best that modern medical science offers in diagnosis and therapy. This group idea is the logical and inevitable evolutionary product from an age of intensive specialization, and it has come to stay.

It seems to me, therefore, fundamentally important that the profession should be kept fully informed regarding the significance of the disorders encountered in the various special domains, particularly with reference to their disturbing influence upon the proper functioning of the organism as a whole, in order that wise judgment may be exercised in the matter of choosing consultants and of rendering efficient service to the individual patient. To this end it is my purpose in this communication to show that urogenital disorders in women are so prevalent nowadays and their pernicious influence upon the female organism as a whole is so real and so profound that a careful examination by a competent gynecologist can not with impunity often be omitted from any general diagnostic study of a woman that purports to be reasonably thorough and complete. The space at my disposal, however, will permit me to discuss briefly only a few of the many groups of abnormalities encountered by the gynecologist which might be presented in support of my thesis.

THE PRE-ADOLESCENT PERIOD

Among the various disorders of the genital apparatus in the female commonly met with before puberty, physicians would do well to keep two conspicuously in mind. The first of these is gonorrhea. It does not appear to be generally appreciated by the profession that this disease is fully as contagious among female children as is measles or scarlet fever. Not uncommonly several children in one family between the ages of six months and twelve years are found to be suffering with it in its most virulent form, and numerous instances are on record of an epidemic of it having swept through an entire female children's ward or orphanage within a week or ten days. Traced to their source, the overwhelming majority of cases are found to have been contracted from the toilet seats of public schools or other institutions, or from bath tubs, towels or the hands of attendants which are contaminated by gonococci. The importance of recognizing this disease as soon as the symptoms of vulval irritation appear can not be exaggerated. Its proper treatment usually requires a two-stage therapy, both of which require tact, skill and persistent effort. The first stage is occupied in gaining the confidence and co-operation of these little patients, who uniformly have been repeatedly terrified, not to say persecuted, by the altogether senseless procedure—unfortunately

often advised by physicians—of having been forcibly held while a pseudo-vaginal douche was administered. The effective use of an antiseptic vaginal douche in a screaming, struggling child is manifestly impossible and gentle bathing of the external genitals will remove the purulent discharge from the vulva just as thoroughly and with far less insult to the nervous system of both mother and child. The curative therapy begins in the second stage when, after having gained the child's confidence, the knee-chest posture is made use of to effect a ballooning of the vagina under atmospheric pressure. The vaginal introitus is rendered less sensitive by the application for a few moments of a cotton pledget saturated with 4 per cent. cocaine; a soft rubber catheter is then gently introduced, and a thoroughly satisfactory irrigation with a warm antiseptic solution is given. Oftentimes, too, a Kelly cystoscope is introduced and through it a thorough application of silver nitrate to the cervix is easily and satisfactorily accomplished.

A second genital disorder commonly encountered in female children and capable of producing disturbances of a most serious character is that of an adherent prepuce with an accumulated mass of incarcerated smegma closely packed about the clitoris. For let it be remembered that this organ is a highly sensitive structure composed of erectile tissue and richly supplied with nerve fibres, and that when it is subjected to the constant mechanical irritation just described a vicious circle of immeasurable significance from a neurological standpoint is set into operation. To what extent this condition may lead to erroneous diagnosis and lamentably harmful therapeutic effort three recent cases encountered in my own practice will serve to illustrate. All three of these patients belonged to families of affluence and high social position. One of them, a little girl eleven years of age, had grown up from infancy annoyed and humiliated by the distressing habit of nightly bedwetting. She had been perennially dieted, drugged, restricted with regard to fluid intake and aroused at intervals during the night to void, all of which measures served only to foster a nervous, irritable, unattractive temperament and nearly made a wreck of her mother. Examination disclosed an unusually redundant prepuce with a mass of incarcerated smegma beneath. Circumcision terminated the nocturnal enuresis overnight and, within a week, completely transformed the temperaments of both child and mother. The two other cases were almost identical in their main features. Both were charming little girls of about ten years of age whose homes and social environment left nothing to be desired. Contrary to appearances, however, each had been adjudged an intractable masturbator. In each instance the advice of a cotorie of the most eminent pediatricians, neurologists and internists of this country had been successively sought with the result that a formidable list of polypharmacy, dietary regimes, rest cures, diversions by way of trips to fashionable health and pleasure resorts under the constant care of professional nurses, together with disciplinary educational systems, had been faithfully tried for months. The havoc thus wrought both temperamentally and nervously, as well as physically, was only too apparent to the experienced observer, while the concern, gloom and humiliation of their parents was indeed pathetic. A simple circumcision in each case, together with removal of the mass of incarcerated smegma packed about the clitoris, promptly disproved the diagnosis of habitual self-abuse and, more important still, relieved the nervous systems of these little girls of a strain severe enough to have already caused marked functional derangements.

THE POST-ADOLESCENT PERIOD

One of the commonest groups of pelvic disorders responsible, through psycho-neurotic and functional disturbances, for remotely harmful influences of sufficient degree to discount materially the efficiency of a woman is that embracing the various degrees of mechanical injury incident to childbirth. For a number of years I have been convinced and have been teaching medical students that permanent damage to the various anatomical structures, composing and adjacent to the birth canal, of sufficient degree to produce later a sequence of symptoms of vital significance

to the health and well-being of the woman, is not the exception but the rule even in normal deliveries. I want to state emphatically and unequivocally as my deliberate judgment that it is not mechanically possible for a normal size full-term child to descend through the birth canal of a normally developed woman—no matter by how experienced an obstetrician or under however ideal conditions the labor may be conducted—without leaving permanent injury of sufficient degree as not only to be later readily demonstrable, but also, in most instances, to be directly responsible for a group of symptoms which materially discount the efficiency of the woman. I am fully aware, of course, that at present such radical teaching will receive few, if any, supporters, especially when I make haste to add that I have had very meager obstetrical experience. For no fallacy is more firmly fixed in the minds both of the profession and of the laity than that obstetrical injuries constitute one of the unpardonable sins and brand the attending physician as incompetent: as witness, on the one hand, the resentment depicted in the face of a woman when, after a pelvic examination, she is informed that she was injured in childbirth; or, on the other, the occasional echo from by-gone days still heard at the meetings of some county medical societies under the modest caption of "One Thousand Deliveries Without a Tear."

The permanent damage to which I refer has to do not with the superficial lacerations of the vaginal mucosa, the hymen, the fourchette or even the sphincter vaginæ and minor perineal muscles. These usually are repaired with scrupulous care at the time of delivery. But what I am trying now to emphasize is that the really significant injuries include stretching of the supporting ligaments of the uterus, lacerations of the cervix, and particularly submucous stretching and tearing of the highly important subvesical fascia and of the levator muscle fibres, together with their encasing fascial layers. The extent of the trauma to these structures usually is not apparent at the end of the puerperium, even to an experienced observer, since weeks or months must elapse before the atrophy, which inevitably follows, is complete. Later on, however, especially in multipara and as the menopause age is approached, there develops the familiar clinical syndrome indicative of a relaxed outlet with varying degrees of descensus of the pelvic viscera. And then, in turn, follows the associated picture of a nervously bankrupt woman, whose life is made miserable, whose beauty and attractiveness are gone and whose efficiency is a minus quantity by reason of a multitude of disordered organic functions. I can not emphasize too strongly that a thorough pelvic examination should occupy a prominent place in the diagnostic study of every parous woman, no matter how remote from the pelvic domain her complaints may appear to be.

During recent years the intensive study of the glands of internal secretion has given us, among other things, a much broader and more comprehensive idea of the functions of the ovaries. Formerly these organs engaged our attention chiefly with reference to their surgical removal for reasons both real and fanciful but, in the light of recent investigations, we must recognize now that they constitute one of the most important units of the entire endocrine system, since they not only govern the functions of menstruation and reproduction but, in addition, exercise a profound influence far afield from the genital domain. The perfectly co-ordinated cyclic phenomena which culminate each twenty-eight days in the fully developed corpus luteum in the ovary and the menstrual flow from the uterine mucosa furnish one of the most beautifully adjusted physiological mechanisms of the entire human organism. Furthermore, it serves to remind us of the fact that the ovaries are complex glandular organs which are continuously active in the elaboration of one or more specific internal secretions of a highly important character. The exact structure and chemical reactions of these products within the body are still imperfectly understood, but that through them the ovaries are brought into very intimate physiological interrelationship with various other endocrine units has been convincingly demonstrated. Thus, for example, it has been clearly shown that normal development of the whole group of

secondary sex characteristics which occurs at puberty is dependent upon normally functioning ovaries; so, too, we are familiar with the temporary enlargement of the thyroid gland commonly observed at puberty and during pregnancy; and with the profound and complex disturbances—partly traceable to functional derangement of the autonomic nervous system and partly psycho-neurotic in type—which are associated with the menopause; while, conversely, it is a well established fact that primary disease of the pituitary body or of the thyroid gland is frequently responsible for functional, and possibly also for developmental, anomalies of the reproductive organs. It is evident, therefore, how important it is to determine through a careful pelvic examination the condition of the ovaries as a part of the general diagnostic study of woman.

One of the commonest pelvic symptoms encountered is that of abnormal uterine bleeding, but its full significance is certainly not appreciated by the profession at large. From the best available statistics it is probable that at least twelve thousand women die annually in the United States alone from cancer of the uterus. All of us know that the only certain cure for this disease is its early and complete surgical extirpation while it is still localized.

Some years ago an analysis of the uterine cancer cases in the Gynecological Department of the Johns Hopkins Hospital showed that in over 60 per cent. of them there was a history of neglected uterine bleeding which had been going on for over six months, and during the past thirteen years, covering the period of my active participation in the work of this Clinic, I am sorry to say that I have observed no improvement in this direction. Now, when we consider that three-fourths of the patients afflicted with cancer of the cervix die within two years, and one-third of them within one year from the initial symptom, the importance of early diagnosis and prompt surgical treatment becomes apparent.

This distressing situation with reference to uterine cancer is to be attributed mainly, I believe, to two erroneous ideas which are still firmly fixed in the minds of both the profession and the laity; one is that cancer does not occur until after thirty, and the other is that any kind of abnormal uterine bleeding is to be expected at the menopause age, and, therefore, need not be regarded seriously when it occurs. Heaven only knows how many women have died from uterine cancer as a result of these two fallacies. I have seen inoperable cancer of the cervix at every period of life from the early twenties to extreme old age. Let me emphasize, therefore, that the age limits in this disease extend from puberty to death.

Unfortunately, pain is not a symptom of cancer of the uterus, text-books to the contrary notwithstanding. Rather it is to be considered one of the first signs of death, for uncomplicated cancer of the uterus produces not a twinge of pain until it has extended beyond the uterus and become incurable.

There is but one symptom to remember in connection with the early stage of this disease and that is slight abnormal uterine bleeding. That is all. Not a hemorrhage; no sudden gush of blood; nor even a continuous seepage; but only a slight staining from the little oozing that follows the breaking down of a few epithelial cells. This is the first and earliest sign of uterine cancer. Does the significance of this fact strike the reader with its full force? Would that I could herald the message abroad throughout the length and breadth of our land in such stentorian tones that every doctor and every woman within its bounds would realize and respond intelligently to the unalterable fact that *every case of abnormal uterine bleeding, however slight and at whatever age, means cancer until proven otherwise through an exhaustive examination by a competent physician!* But I have said enough to emphasize the importance of a pelvic examination as a part of the diagnostic study of every woman presenting this symptom.

One of the epoch-making advances in medical science has been the demonstration within recent years from the standpoint of pathological physiology of the baleful influence of concealed foci of infection within the human body. The pitiless spotlight of scientific investigation

has been relentlessly focused upon infected teeth, tonsils, paranasal sinuses, gall-bladders and appendices until even the most skeptical among us can not possibly longer entertain any doubt as to their causal relationship to a group of diseases formerly imperfectly understood and unsatisfactorily treated. By the same process we are beginning to realize now that pelvic infections belong in the same iniquitous category. There may be nothing particularly startling in the isolated fact that tuberculous peritonitis in women more frequently spreads from foci in the Fallopian tubes than from any other anatomical site; neither are we often so acutely sensible as might be desirable of the prolonged morbidity and remote havoc brought about by puerperal sepsis following imperfect obstetrical technique and the ever-multiplying and nefarious acts of criminal abortionists; while so accustomed had we become to hearing of the prevalence of gonorrhea and syphilis that it required nothing less than a world war and the amazing disclosures of the medical examining boards of our Army and Navy which it occasioned to arouse us from our professional lethargy and to bring home to us the undesirable fact that these venereal diseases seriously threaten the very life of our Nation, and that their eradication constitutes one of the greatest and most imperative public health problems of all ages.

Consider, then, if you please, the collective incidence today of tuberculous, of puerperal and of venereal infections of the female reproductive organs, reflect upon their unparalleled significance as foci of infection not only to the individual woman but also to her pitiable offspring and to the public health, and nothing more need be said, I am sure, to stress the importance of a specific search for these diseases as an essential part of the diagnostic study of every woman.

So intimately bound up with the diseases of the female genital system are the surgical disorders of the urinary tract that the two, of course, are inseparable. But, thanks to modern urological methods of investigation and especially to the Kelly open-air mode of cystoscopy, a complete and accurate study of the urethra and bladder, an investigation of the ureters particularly for the presence of strictures and calculus, capacity and contour details of the renal pelvis, as well as a comparative study bacteriologically, chemically and functionally of the two kidneys, all may now be accomplished with the utmost ease at a single brief examination. Bladder symptoms are almost as prevalent among women as is backache. Ureteral strictures in women we now know to be a common disorder and responsible for many useless laparotomies for supposed disease of the ovaries, appendix or gall-bladder. Urethritis, cystitis, bladder ulcers and neoplasms, pyelitis, calculus and tuberculosis of the urinary tract are always with us. So that a cystoscopic study is often the most illuminating part of a pelvic examination and, hence, must be frequently resorted to in the general diagnostic study of women.

The space at my disposal does not permit me to discuss the relationship to the female organism as a whole of the benign tumors of the uterus; of the varied neoplasms of the ovaries; of the abnormalities of pregnancy, including the ectopic cases; of the problems of sterility and sexual inequalities; of the almost constant association of pelvic diseases with surgical abnormalities of the abdominal viscera — including the appendix, the intestines, the stomach, the gall-bladder and the rest. But if I have succeeded in focusing the attention of the reader upon the prevalence, the scope and the significance of urogenital disorders, upon their injurious effects upon the health of the individual and upon the attention which they merit in every thorough general diagnostic study made of a woman, the purpose of my communication has been achieved.

1200 *N. Charles St.*

EYE, EAR, NOSE AND THROAT

A CASE OF KERATITIS PROFUNDA (OR DISCIFORMIS?) WITH MICROSCOPIC EXAMINATION*

By F. H. Verhoeff, A.M., M.D.,
Assistant Professor of Ophthalmia Research, Medical Department,
Harvard University,
Boston, Mass.

Although it is possibly somewhat uncertain whether the case I have to report should be classified as one of keratitis profunda or of keratitis disciformis, our knowledge regarding the true nature of either of these conditions is so indefinite that the histological findings in my case would seem to be of considerable importance. The case occurred at the Massachusetts Charitable Eye and Ear Infirmary on the service of Dr. F. M. Spalding, to whom I am indebted for the privilege of reporting its clinical features.

CASE REPORT

Benjamin, H. N., aged 65, a stableman, was admitted to the Massachusetts Charitable Eye and Ear Infirmary, January 2, 1915. The patient stated that his left eye had been affected for the previous three weeks. The vision had become blurred, and the eye had felt irritated, but there had been no actual pain.

EXAMINATION

Right eye normal: vision 20/30; tension 17 mm. (Schiotz). The left eye was considerably congested. The cornea was markedly hypesthetic and had a distinctly grayish hazy appearance, with general unevenness of the surface, probably due to edema, but it did not stain with fluorescine. The anterior chamber was normal in depth. The pupil, normal in size, reacted poorly to light. The iris' markings were slightly blurred. The corneal condition obscured the view of the fundus. Tension, 35 mm. (Schiotz); vision, fingers at 1½ feet. Solution of pilocarpin nitrate 1 % was ordered to be instilled three times daily.

BEDSIDE NOTES

January 10.—Left eye painful and more congested. Pupil contracted and irregular. There appear to be some deposits upon the posterior surface of cornea.

January 11.—Atropin sulphate 1 % is substituted for pilocarpin.

January 13.—Pupil is dilated and irregular from posterior synechiae.

January 17.—Tension lower. Pupil half dilated. Deposits on the posterior surface of the cornea persist.

January 24.—There is less pain. The cornea is still quite hazy.

January 31.—Some blebs are still seen on the cornea as in bulbus keratitis. Tension only slightly elevated. Some pain at times.

February 7.—There is very little pain. The cornea is roughened and hazy. There is moderate congestion.

February 21.—The tension is normal.

February 25.—There are two spots in the upper part of the cornea that stain with fluorescine. There is very little pain. Tension is normal.

February 28.—There is some superficial vascularization of the cornea above. The pupil is moderately dilated.

March 21.—The eye is more congested. The cornea is very hazy. Enucleation is advised.

March 22.—Enucleation of the left eye under local anesthesia by Dr. Lancaster, eleven weeks after the onset of the keratitis.

PATHOLOGICAL EXAMINATION

(3-2789.) Fixation in an aqueous solution containing formalin 10 %, alcohol 54 %.

Macroscopically.—The globe is normal in size and shape. The cornea is clouded by the method of fixation so that no details can be made out within it. Its surface is smooth and is covered with epithelium. There is a vascularized pannus all around, most marked above. The anterior chamber is slightly shallow, and contains a delicate serous coagulum. The lens is *in situ*. The filtration angle is everywhere free. The pupil is 3 mm. wide, and its margin is firmly adherent to the lens. The vitreous is normal. The retina and choroid are *in situ* and are apparently normal. The disc is not swollen nor noticeably cupped.

Histological Examination.—Fixation was accomplished as noted above. Meridonal vertical sections were made through most of the central portions of the cornea, and plane sections through the remaining central portion. Longitudinal sections were cut through the optic nerve nearly to the central vessels and serial cross sections were made of the remainder of the nerve. These were stained in hematoxylin and eosin and in a variety of other stains.

The most marked corneal changes involve a central area about 4.5 mm. in diameter (Fig 1). Here, in the anterior third of the corneal stroma, the lamellæ have become slightly hyaline in appearance and have lost their distinct outlines, while the corneal corpuscles have completely dis-

*Read before American Ophthalmological Society, Atlantic City, June 16, 1919.

From the Massachusetts Charitable Eye and Ear Infirmary.

appeared. In fact, no cells of any kind are present here (Fig. 2). Posteriorly, the corpuscles become visible in small numbers, many of them, however, showing chromatolysis, pyknosis, or fragmentation of their nuclei, and others, active proliferation. Just in front of Descemet's membrane, in a sharply defined layer about one-seventh the thickness of the cornea, the corneal corpuscles are greatly increased in number; their nuclei are rich in chromatin; and many of them show various stages of amitosis or mitosis. At the periphery of the central area, this layer of proliferating corneal corpuscles extends away from Descemet's membrane and rapidly becomes broadened out and disappears. The corneal stroma shows no vascularization, and is almost free from leucocytic infiltration throughout, except near the limbus where there is slight infiltration with pus cells.

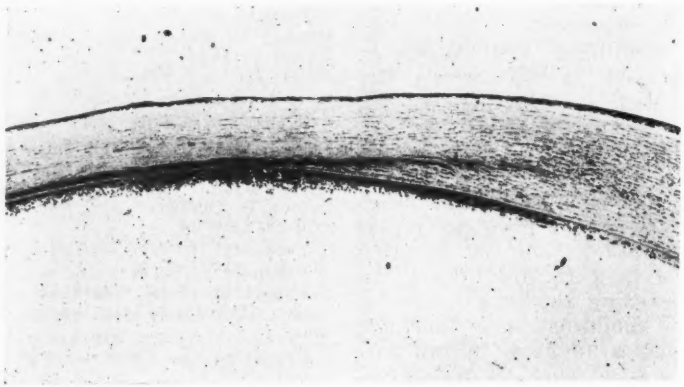

Fig. 1.

Median vertical section of cornea, including upper half of affected area. (The other half of the area not included in the photograph presented a similar appearance.) The epithelium is intact, but altered. The anterior layers of the central portion of the cornea are devoid of nuclei. In front of Descemet's membrane, the corneal corpuscles have actively proliferated, forming a layer which rapidly widens out and disappears at the periphery. In the middle layers of the cornea, some of the corpuscles are in various stages of necrosis, others are in active proliferation. There is no infiltration with leucocytes. The endothelium is absent, and the posterior surface of the cornea is coated with fibrin and leucocytes. Hematoxylin and eosin. Photo x 41.

In this central portion, the cornea is reduced to about two-thirds its normal thickness, probably owing to shrinkage and compression of the injured tissue resulting from the action of the fixing fluid employed. Bowman's membrane is everywhere intact. The epithelium is normal at the periphery of the cornea, but over the central portion it is greatly altered. Here it is thinned, due to changes affecting the basal cells, the squamous surface layers being intact. The basal cells are shrunken and distorted, and their nuclei are often pyknotic. Many of the pyknotic nuclei are stretched out into irregular fantastic shapes. These changes are best seen in plane sections. In places there are small cystic spaces beneath the intact surface layers, containing discrete altered basal cells that have been cast off from Bowman's membrane.

Descemet's membrane is also everywhere intact. The endothelium is completely absent behind the central portion of the cornea, a stretch of 1 mm. of it remaining at the periphery below and 4 mm. above. Behind the central area there is a layer of fibrin and leucocytes, about .04 mm. thick and 4.5 mm. in extent. Immediately in contact with Descemet's membrane the leucocytes consist almost exclusively of pus cells; the other cells enmeshed in the fibrin are chiefly endothelial cells, many of them containing pigment. Occasionally one of the endothelial cells is multinucleated. Many fibroblasts are also seen, indicating that organization has begun. Towards the periphery the layer of fibrin ends rather abruptly, but considerable numbers of pus cells and small and large lymphocytes are adherent to the cornea all the way to the filtration angle. About 5 % of the polynuclear leucocytes are eosinophiles.

In addition to the large central corneal lesion just described, two smaller spots evidently of the same general nature are encountered. The spots are similar in character, but the sections pass through the center of only one of them. The latter is about .75 mm. in diameter. Within it the corneal corpuscles beneath Bowman's membrane for a depth of 3 or 4 lamellæ show marked pyknosis and pigmentation, while those still deeper are greatly increased in number and their nuclei show various stages of amitosis and budding. In this vicinity the stroma shows a slight infiltration with pus cells. Over the center of

this spot the epithelium is markedly altered. The basal cells have disappeared as a definite layer, and the surface layers are lifted up, leaving a cystic space filled with discrete cells. The latter have only a small amount of cytoplasm, possess small nuclei of various sizes, and seem to have been derived from basal cells that have been cast off from Bowman's membrane. Intermingled with these cells there are also a few pus cells.

The tissue of the limbus is highly congested and greatly thickened by infiltration with chronic inflammatory cells, chiefly plasma cells. Extending between the epithelium and Bowman's membrane from above for 2.75 mm. there is a pannus somewhat similar in appearance to a pannus degenerativus. This is actively growing and is richly infiltrated with chronic inflammatory cells. A similar pannus is beginning below. A few vessels are just beginning to push their way from the sclera into the deeper layers of the cornea.

The filtration angle is nowhere blocked by the root of the iris. Below it is filled with leucocytes up to the level of the end of Descemet's membrane, and also contains a small amount of fibrin. Pus cells predominate here, but there are also many plasma cells, lymphocytes and a few endothelial cells. The spaces of Fontana are filled with similar cells. A few new formed capillaries are making their way over the surface of the ligament, some of them beginning to extend over the posterior surface of Descemet's membrane. The serum filling the anterior chamber contains scattered leucocytes, about 6 to 12 to the high power field.

The iris is considerably infiltrated with chronic inflammatory cells, chiefly lymphocytes, but is not highly congested. The infiltration is greatest in the region of the sphincter, where it tends to assume a nodular character. Along the anterior surface of the iris are numerous leucocytes, mostly lymphocytes, but almost no fibrin. There is an annular posterior synechia 1 mm. wide. From the pupillary margin there extends a thin fibrous membrane over the surface of the lens, blocking the pupil. Over the central portion of this membrane there is a layer of fibrin in which a few leucocytes are enmeshed.

The ciliary body is almost normal, showing only a slight leucocytic infiltration. The retina and choroid are normal. The optic disc is possibly very slightly cupped. The central vessels, cut in serial cross sections, are normal. The lens is practically normal, showing only slight cataractous changes at its periphery.

Bacteriological Examination.—Sections stained by the Gram method, the method for tubercle bacilli, and in carbol-thionin, show no microorganisms in the cornea nor elsewhere.

REMARKS

This case was not seen by me clinically, and the clinical notes upon it were made by a house surgeon unfamiliar, naturally enough, with such rare conditions as keratitis disciformis and keratitis profunda. The clinical description, therefore, is not sufficiently detailed for a diagnosis to be made from it alone, but interpreted and

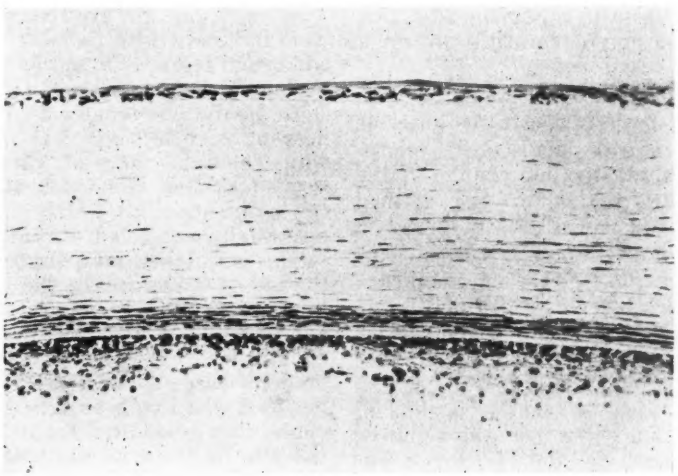

Fig. 2.
Section of central portion of affected area of cornea under higher magnification. Hematoxylin and eosin. Photo x 150.

amplified in the light of the microscopic findings it shows that clinically the cornea displayed a grayish circular opacity 4.5 mm. in diameter. Over this the epithelium was intact, but presented a marked stippling of its surface, and on one occasion, vesicles. The margin of the opacity must not have been sharply defined, but was intensified by the zone of proliferating corneal corpuscles surrounding the main opacity. It is doubtful that this was sufficiently conspicuous clinically to form the intensified border described by Fuchs as characteristic of disciform keratitis. The thick layer of fibrin and leucocytes, however, on the posterior surface of the cornea had an extremely sharp peripheral outline, and may well have given a disciform appearance to the whole opacity as seen clinically. In addition to the central opacity there were two outlying superficial punctate spots, both of which were also seen microscopically. Both clinically and microscopically there was noted severe iritis with posterior synechia and deposits on Descemet's membrane.

From these facts it is obvious that this case was either one of keratitis profunda or of keratitis disciformis.

The opacity of the cornea was, no doubt, primarily due to alteration in the anterior layers of the cornea manifested microscopically by slight hyaline change of the lamellæ and destruction of the corneal corpuscles. Later it was greatly increased by the layer of proliferating corneal corpuscles in front of Descemet's membrane and by the thick layer of fibrin and leucocytes deposited on the back of the cornea. The changes in the epithelium in this case were most striking. Just how much importance to attach to them it is difficult to determine, since the eye was removed under local anesthesia and the cornea was exposed to drying and the action of cocaine for an unusual length of time. The distortion of the nuclei was almost certainly due chiefly to this cause. The other changes, however, were probably not artefact because they existed only over the affected portions of the stroma, namely, over the central area and over the small punctate spots at the periphery. Moreover, I have never seen such changes in any other eye removed under local anesthesia.

In the literature, no case diagnosed as keratitis profunda, and only two cases clinically diagnosed as disciform keratitis have been examined microscopically,—one reported by Hadano,[1] the other by Meller.[3] Hadano examined only a piece of tissue removed from the cornea by means of a sharp spoon, while Meller examined the entire eye. The findings in these two cases were so different that it is almost, if not quite, impossible to believe that the two cases represented similar conditions. Thus Hadano found that the small piece of tissue removed by him (he does not mention its exact size) consisted of a swollen mass of wavy interlacing bundles in which there was complete absence of inflammatory infiltration or tissue proliferation. Only a few nuclei were to be seen, and in the central area almost no nuclei were present. On the other hand, Meller found intense cellular infiltration with necrosis of the infiltrate and loss of corneal substance.

In my case, the microscopic findings were in accord with those of Hadano. The additional features found by me could not, of course, have been seen by Hadano, because he did not remove a sufficient thickness of corneal tissue to reveal them, while the appearance of wavy bundles described by him is no doubt explained by the traumatism to which the tissue was necessarily subjected during its removal.

The possibility may suggest itself that the changes present in the cornea in my case existed in Meller's case, but were masked by a secondary infection. Careful examination, however, of sections from Meller's case, which were kindly sent to me by Prof. Fuchs several years ago, excludes this possibility, for in these sections there is no trace of the hyaline condition of the corneal stroma nor of the layer of proliferating corneal corpuscles which in my case walled off the central area from behind and also formed a peripheral zone around it.

As pointed out, my case was certainly one of keratitis profunda or disciformis. Meller's case was just as certainly not one of keratitis profunda, for the great density of the corneal infiltration as well as the

relatively extensive loss of corneal substance excludes this possibility. If, therefore, we assume that disciform keratitis is a distinct entity, and that Meller's case was a true case of this condition, we must conclude that my case and that of Hadano were cases of keratitis profunda. I am, however, not prepared to make either one of these assumptions.

As a matter of fact I am convinced that the cases of disciform keratitis described in the literature do not represent a single condition. Disciform opacity of the cornea may arise from a variety of causes. As is well known, it may occur in hereditary syphilis where it probably is due to a metastatic infection of the cornea with spirochetes, it may occur as a type of *ulcus serpens*, it may result from infection with vaccine virus, as pointed out by Schirmer,[3] it may occur in non-gonorrheal ophthalmia neonatorum due to infection with the *Streptococcus mucosus* as I have myself observed. Probably it may occur as a form of tuberculosis of the cornea as suggested by Weeks[4], and as a result of unknown infections. Finally, it may occur as a complication of herpes cornea or as a result of trauma, in which cases it is probably neuropathic in origin as maintained by Peters, although Fuchs' view that here also it is due to some unknown infection has not been excluded.

Possibly the cases of keratitis disciformis originally described by Fuchs did comprise an entity, but his clinical description is not sufficiently exact, and probably no description based upon clinical appearances could be sufficiently exact to enable other observers to identify the condition with certainty. Moreover, such cases are seen by any one observer at such long intervals that it is unlikely that the clinical picture could often be carried in mind from one case to another. In the clinical description of his case, Meller states that after a time the infiltrate presented a sharply-defined margin, but he does not mention here the intensified border described by Fuchs as characteristic of disciform keratitis. He does, however, attempt to reconstruct the clinical appearance from his microscopic findings, but in my opinion he fails to do so successfully. One of the sections of his case in my possession passes near the middle of the infiltrate, yet it fails to show anything which would give the appearance of an intensified border. His illustrations likewise fail to do so. In two other ways also his case did not conform to Fuchs' description, namely, in that the density of the infiltrate was unduly great for the small size of the latter and in that the loss of substance was relatively large. For, from measurements made from the section referred to, and from the illustrations of Meller's case, I find that the infiltrate was only 2 mm. in diameter and the loss of substance involved half of this area. Owing to the necrosis of the infiltrate Meller was unable to determine the nature of the cells comprising it. It seems to me, however, that I can identify many of the cells as endothelial phagocytes and to determine definitely, at least, that the infiltrate does not consist chiefly of pus cells. This is substantiated by the fact that almost no pus cells are approaching it from the periphery. From the foregoing considerations I conclude that Meller's case, although not one of keratitis profunda, was not a typical case of disciform keratitis as described by Fuchs, and that it was not due to tuberculosis or to vaccine virus, but probably to infection of the cornea with some unidentified non-pyogenic micro-organism.

The term keratitis profunda has been used in a general way for many years to describe various forms of deep-seated keratitis, including that of hereditary syphilis, but so far as I can ascertain Fuchs was the first to restrict its use to a distinct clinical entity. In his latest textbook (Duane's translation) he makes the following statement in regard to the differentiation of this condition from keratitis disciformis:

> "Keratitis disciformis has a certain resemblance to keratitis profunda, in which also a deep-seated gray, non-ulcerating cloudiness develops in the center of the cornea. But this is composed of gray striae and specks and merges gradually into the transparent cornea. In keratitis disciformis, on the contrary, the opacity appears uniformly gray and only on strong magnification is resolved into very minute clear-cut, white, closely packed dots; moreover, it is very sharply demarcated from the healthy cornea by the gray circular line along its border."

Taken in connection with his detailed description of the two conditions, it seems to me that the points mentioned by Fuchs are not always sufficiently definite, and I therefore concur in the view of v. Hippel[5] that it is not always possible to differentiate the two conditions. In other words, I believe there are cases which present the essential clinical features of disciform keratitis but which are really of the same nature as keratitis profunda, and it is to this class of cases to which I believe my case and that of Hadano belong. This view harmonizes with the following statement made by me[6] ten years ago:

"The facts that both keratitis profunda and keratitis disciformis occur most commonly after herpes zoster or trauma, that both may be associated with corneal hypesthesia and show outlying superficial punctate spots, impel me to believe that both conditions are essentially neuropathic, the minor differences between them being dependent upon differences in the intensity of the nerve irritation."

The question now arises as to the indications the histological findings in the present case offer in regard to the cause of the condition, and as to whether or not these findings support the clinical evidence that keratitis profunda is neuropathic in origin. In the first place it is obvious that the central corneal lesion is due to some diffusible toxic substance arising in the anterior layers of the cornea. This is evident from the fact that the corneal corpuscles have been completely destroyed in the anterior third of the cornea and are progressively less injured from before backward, while next to the membrane of Descemet and at the periphery they have been stimulated by the weakened toxin into active proliferation. Likewise, the corneal lamellæ are most affected anteriorly. That this toxin was of infectious origin is highly improbable. For it seems almost impossible for organisms to have existed in the cornea for eleven weeks without causing leucocytic infiltration of any kind in the affected area. It is true that highly virulent organisms often produce toxins of such intensity that the latter prevent leucocytes from reaching the site of infection, but in such instances the area is always surrounded by a zone of leucocytes and the infected tissue undergoes necrosis and breaks down. In the present case, the corneal corpuscles were destroyed in the affected area, but the stroma was only slightly injured, while the cellular infiltration even of the surrounding cornea was insignificant.

On the other hand, the histological findings in the present case are in perfect accord with the theory of neuropathic keratitis advanced by me in 1909 and again in 1911.[7] According to this theory, as a result of an irritative lesion in the gasserian, or possibly the ciliary ganglion, impulses are sent backward to the nerve terminals in the cornea where they produce electrolytic changes leading to the formation of toxic substances. The latter then give rise to corneal lesions, chiefly superficial, which vary in character according to the intensity and duration of the nerve lesion and the distribution in the cornea of the nerves corresponding to it. Thus a diffuse lesion in the ganglion involving the nerve supply of the central portion of the cornea would give rise to toxic substances at or near the surface of the cornea which in diffusing backward would produce the changes described. The associated iritis could be explained either by the action of these toxins upon the iris, or by a simultaneous involvement of the nerves of the iris. The deposit of fibrin and leucocytes on the posterior surface of the cornea is easily explained by the destruction of the endothelium by the toxins diffusing through the cornea, just as are explained the mural thrombi that are formed in veins when the endothelium is injured. Had it existed sufficiently long, no doubt it would have undergone complete organization.

The only previous case of neuropathic keratitis of any kind, uncomplicated by infection, in which the entire eye was examined microscopically, was the case of superficial punctate keratitis reported by me in 1911.[7] The punctate spots in this case were situated just beneath Bowman's membrane and showed necrosis of the cornea corpuscles as in the lesions of the present case, but in addition were densely infiltrated with polynuclear leucocytes also in various stages of necrosis. The corneal lamellæ were only slightly injured and there was some proliferation of corneal corpuscles at the periphery of the spots. In both cases the epithelium over

the lesions was altered but not destroyed. Aside from differences in size, therefore, the only important difference between the corneal lesions in these two cases consisted in the far greater leucocytic infiltration of the lesions in the earlier case. Three possible explanations for this difference suggest themselves:

1. That the leucocytes of the patient in the present case were less sensitive to the chemotactic influence of the toxic substances diffused from the cornea, although in both cases these toxic substances were the same in kind.

2. That in the first case the toxic substances were produced more rapidly and hence were more concentrated in their action. This is in accord with the fact that at the time of enucleation the duration of the lesions in the first case was about 3 weeks; in the present case, 11 weeks.

3. That early injury to the endothelium in the present case caused the diffusion of the toxins to take place chiefly into the anterior chamber. This is in accord with the fact that an abundance of polynuclear leucocytes were enmeshed in the fibrin on the posterior surface of the cornea.

Assuming that the present case was one of keratitis profunda, it is obvious from the microscopic findings that this term is misleading. For, while the deeply-seated changes in this form of keratitis are clinically the most conspicuous, it is obvious that the toxic substances which cause them arise at or near the surface of the cornea.

CONCLUSIONS

Disciform keratitis may be produced by a variety of causes, and from an etiological standpoint is therefore not an entity.

Certain cases of disciform keratitis are of the same nature as keratitis profunda.

The corneal changes in keratitis profunda are due to the action of diffusible toxic substances arising near the anterior surface. The changes consist in alteration of the epithelium, destruction of the corneal corpuscles and injury to the stroma in the anterior layers of the cornea, and proliferation of the corneal corpuscles behind and around the injured area. In addition to this, there is injury to, or destruction of the endothelium, and in severe cases, deposition of fibrin and leucocytes on Descemet's membrane behind the affected area. Leucocytic infiltration of the corneal stroma is conspicuously absent.

The microscopic findings in the present case strongly indicate a neuropathic origin for keratitis profunda.

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BIOGRAPHY

ROBERT PEMELL, A PEDIATRIST OF THE PROTECTORATE

By John Ruhrah, M.D.,
Professor of Pediatrics, University of Maryland and College of Physicians and Surgeons,
Baltimore, Md.

In the middle of the seventeenth century there flourished a large number of medical worthies about most of whom we have a fairly accurate knowledge. This was the time of Glisson, whose work on rickets appeared in 1650; of Harvey; of Highmore of antrum fame; of Thomas Willis; of the great Sydenham; and of John Mayow. In this century Leeuwenhoek, Sylvius de le Boe, Malphighi, de Graaf, and other masters contributed their discoveries. There were countless others, most of whom left no trace behind, or, if any, it has been buried in the dust of the library. To fix the period better, perhaps, it may be mentioned that it was the age of Louis XIV in France and of the Protectorate in England, and that in 1653 Oliver Cromwell was made Lord Protector of the Commonwealth.

At this time Cranbrook or Cranebrooke was a flourishing manufacturing town chiefly concerned in making broadcloth. It takes its name from a stream that runs into the River Beult and is about forty-five miles southeast of London in the County of Kent. From the fourteenth to the seventeenth century Cranebrooke was a place of some importance; since then it has fallen from its high estate to be a market town of about four thousand. In this town, lived and practiced one Robert Pemell, who, in the year that saw Cromwell made Lord Protector, published, on May 29, a little book entitled "De Morbis Puerorum." This book was printed in London by F. Legatt, for Philemon Stephens, at the gilded Lion in Paul's Churchyard. Pemell had previously published four other books, two on simples, one on diseases of the head, and one on "Help for the Poor," but of these, more later.

Concerning Robert Pemell we know nothing whatever except what we glean from his books. His dates are not in the "Index Catalogue" and Leslie Stephen did not think him worthy of inclusion in the "Dictionary of National Biography," or perhaps the editors did not know of his existence. His book is not listed in Meisner's *Grundlage*. Pemell did nothing, as far as can be ascertained, but practice his profession and write five books. His only claim to fame is that he left an excellent account of certain phases of practice as carried on in his day. He deserves credit, too, for writing his works in English, being among the first to break the shackles of scholastic Latin. Not that he was lacking in erudition himself, but he realized that the best way to help the laity and the young physician was to write in the tongue they understood best of all.

We know nothing about Pemell, and yet in 1653 he was getting on in years, for he says: "And because I see my glasse run apace, and I know how short my time is, therefore, I have made the most haste and taken the present advantage."

We know nothing of Pemell, and yet it may be hazarded that he required not more than six or seven hours' sleep, used a large pillow to keep his head high, drank sack and hypocras and did not like such sweet wines as Muscadine or Malmsie.

His first work was entitled

DE MORBIS CAPITIS;
Or,
Of the Chief Internal Diseases of the Head,
with
Their Causes, Signes, Prognosticks, and Cures,
for the benefit of those that understand
not the Latine tongue.
By R. P.

This is a little volume of 141 pages, published by the same Philemon Stephens, this time "at the gilded Lyon," in 1650. Our author is, as he says himself, methodical. His pages bristle with references of the authors consulted, very much like some of us moderns. The margins bear little captions, sometimes in English, but often in Latin. He is a learned man and must needs let others know. His pre-

scriptions are also in Latin and often abbreviated according to the manner of the time. He borrowed freely from the aphorisms of Hippocrates, but he gave credit where credit was due, which is more than can be said of many authors both ancient and modern.

It was not an unpleasant custom of the day to have a poem, usually in Latin, at the beginning of the book. This was generally written by some one else in praise of the volume, or of its author. In "De Morbis Capitis" this was done, the Latin being rendered into English and printed on the following page. This poem is an interesting example of a phase of medical publishing that has fallen into complete disuse:

Concerning

A Book, intreating of the Diseases of the Head, and cure of them; written by Robert Pemell, of Cranebrook, Physitian.

The Head, the Heaven of man's Body is;
The Mind's high Palace, wherein it doth raign;
The Fountain, whence all motion takes its rise,
The Harbour, where the Senses do remain.
As many stars i'th the Sky conjoyned shine;
So rare endowments in the head abound;
Life, Health, Strength, Reason, Wit, do there combine,
And the best Organs of the Soul are found.
If mudless be the Spring, and silver-cleer;
As Silver-cleer, the Streams will also flow:
From muddy Fountains, muddy streams appear;
And like the Fountain, do the Waters go.
Man's health doth much depend upon his head;
If that be sound, th' whole body is at ease;
If that, with illness, be distempered,
On other parts some weakness soon doth seize.
Who then, to skilful Pemell can repay
His due reward? whose care has been so great,
For this chief part, its evills to display,
And of their signs, and Causes, to entreat?
Who likewise hath us of choice Medicines told,
For every Evill's cure, and due relief;
Whatever larger Physick Volumes hold
Good for thy head, is here compriz'd in brief.
Let this good friend be thy Physitian,
Whose skilfull Counsell, and Direction,
Shall either keep thy head in healthfull case;
Or by his Art, away the Evill chase.

JOHN ELMESTON,
School-Master of Cranebrook.

The body of the book starts off with headache and differentiates those aches that are primarily from the brain from those emanating from the stomach, as follows:

"If the pain proceed from the head essentially, there will be no intermission, but a continual pain; or if the pain do remit, it is but little, and returneth again.

"If it proceed from the stomack, the pain will often cease, and return again; also, the appetite will decay; especially, if the stomack abound much with phlegme."

He considers

"Whether Pills do more properly purge the head than other Medicaments?

"It is the opinion of many, that Pills do more properly purge the head, then potions, or electuaries, because they draw more strongly from the remote parts; and also, because they stay longer in the stomack, then the other; which is a truth, but not in regard of the form of Medicine, but because Pills have strong ingredients in them. For there is little reason, that in respect of their form, that therefore lying in the stomack some longer time than other Medicines, they should draw vitious humours, from remote parts; but rather, because the ingredients in those Pills, have a peculiar vertue, to draw the peccant humours from other parts; and so the expulsive faculty is stirred up, and causeth those humours, by the operation of purging Medicine, to be expelled by siege.

"At what time Pills (that purge the head) are to be taken?

"Many are of opinion, that the best time for Pills to be taken, is at night. Now concerning Pills, we must distinguish them thus; some are strong in operation, and have strong purgative ingredients in them; others are gentle, as Pil. stomachic. Ruffi, de hiera, de Aloe, &c. For these, without controversie, the most apt time to administer them, is, one hour after supper; or (as some hold) before supper. But for strong Pils, the most proper time is in the morning fasting, when concoction is perfect; for otherwise, taking such Pills at night, distribution is made too soon, concoction is hindered, and the nourishment, or chylus, not concocted, is carryed into the veins, with the purging Medicine.

"However, I conceive, if the party forbear his supper, or eat a very small supper, he may take these Pills at night, 'though not a full doze at a time, and so for three or four nights together."

After headaches, he considers apoplexy and cites Galen and later writes in the same vein as to the causes, but he gives his own description, a terse little definition, hard to beat in a like number of words:

"Signes of the Apoplexie are these: A sudden crying out, as if they desired help; sense and motion is taken away; sometimes they snort, and lye as if they were in a sleep, and cast spume or froth from out of their mouth.

"Signes of the Apoplexie coming of blood, are these; A redness of the face and eyes; which redness, by reason of the extinction of head, doth turn to green, and at length to blackness; also, the veins of the tongue neer the throat, and the veins of the fore-head, and face, are much swollen.

"Sometimes the sphincter muscle of the Fundement, is so loosened in the Apoplexie, that a glyster can not be reteined, as Sennertus observeth. Pract. med. 1. I. part. 2. c. 33. f. 568."

His treatment of apoplexy is as good as

we have today,—purging and blood letting, but he adds a number of prescriptions of simples to be taken internally and some for external use. These would delight some of our present-day therapeutists, for he was no nihilist. One can not agree with his sternutatious powder in apoplexy, which was to be blown into the nose with a quill, nor with the "oyl of nutmeg chymicall," to be put into the ears and nose. He wisely discourages emesis in the early stage of the disease.

Of the palsies, which he differentiates from apoplexies, he has many suggestions, e. g.:

"An inveterate Palsie is incurable,"

Or

"The Brain of a Hare is much commended in this Disease, as having a peculiar property for the paralyticall."

His observations on convulsions are largely from Hippocrates, eked out with bits of Piso, Leonicenus, Massaria, and other authorities of the time who have passed into oblivion. He pays considerable attention to epilepsy, mentioning the old errors and some of the old truths. His therapeutics and prophylaxis are as extraordinary as those of the present day. The London Pharmacopœia of his day was not made up of unalloyed delights and he commends the following as preventive of the Falling Evill:

"If the child be very young, and you fear this disease, give it so soon as it is born (before it take any thing else) this following:

"℞ Sacchar. alb. ʒ ii. 01. Amygdal. dulc. recent. expres. q. s. f. mixtura instar pultis, cujus usu materia vitiosa in utero collecta in primis viis ejicitur."

The chapters on incubus or Hag or Night Mare, on lethargy, on phrenesie, and mania are strongly tinged with when not taken directly from Galen. For the last named, in addition to numerous prescriptions, he enjoins:

"If the party be bound, give him often cooling and laxative glisters.

"Let not the Patient be left alone, but still have company with him, and let such be his companions, as he loves and delights in, and not such as he hates. Musick is recommended for such. All sweet and delicious meats, and flesh of hot temper, are to be avoided; as also, all manner of Spice."

Pemell wrote two books on simples, the first entitled:

TRACTATUS
De Simplicium Medicamentum facultatibus
A TREATISE
of the
Nature and Qualities of such Simples as
are most frequently used in
MEDICINES,
both purging and others.
Methodically handled, for the benefit of those
that understand not the Latine Tongue.
To which is added:
Many Compound Medicines for most Diseases
incident to Mankinde: As also two Alpha-
betical Tables, very necessary for
the Reader.
Together with,
The Explanations of all hard words or Termes
of Art, whereby the vulgar may better
understand it."

This was printed by M. Simmons, for Philemon Stephens, at the "guilded Lyon" in St. Paul's Church-yard, 1652.

It is delightfully erudite with its long list of authorities and their dates. He starts out:

"Courteous Reader, as the knowledge of Diseases is most necessary and usefull for such as take upon them the Noble art of Physick, so no lesse profitable is the knowledge of simple medicines and their nature: For it is most true; Medicus tantum bene curat, quantum recte cognoscat, he onely cures well that rightly knows diseases and their causes, as also the vertue of simple Medicines, he cures best."

In his preface, entitled "To the kinde Reader," he discusses the choice of medicines:

"Wee ought to give to Cholerick persons those things which purge Choller, to Flegmatick bodies those things which purge Flegme, to Hydropicall that which purgeth water, and to Melancholly persons that which purgeth black Choller or Melancholly."

The purpose of the book is nicely phrased as follows:

"What I have done herein and how methodicall, I have been, I leave to others to judge, for now it is Coram Judice, and surely not without error, for humanus est errare, 'tis incident to the best to erre; some have lapsed herein before me, and others will after me, however let my good will be accepted, which if I finde, I shall be encouraged (God assisting me with life and strength) to publish some other Tracts usefull for the vulgar capacity, as also for young Practitioners."

The first book on simples comprises 170 chapters and the pages are not numbered. Starting with absinthe, he gives a methodical account of various herbs and roots, together with their preparations and uses. While much, if not most of it, is regarded as absurd today, it is not more so than will

be our present-day works on therapeutics in four hundred years. Even less so, one imagines indeed, with our plenitude of vaccines, serums and chemicals. These old fellows sorted and tried out the simples, and while we have discarded most of what they prized, it must not be forgot that the foxglove, belladonna, hyoscyamus and numerous other potent drugs were the direct contribution of the age, just as diphtheria and tetanus antitoxin are among the things of value today and who knows but that even these may be forgot tomorrow in the face of some more efficacious method of treatment as yet undreamed of. So one should read with a sympathetic humor these old books and not deal too harshly with what seem vagaries.

One can not give here much of an account, but some idea may be gleaned from the following extracts. On the use of opium he says:

"Opium is given to provoke sleep, to ease the paine of the Iliack and Collick, as also to mitigate the paine of the stone in the bladder or kidneys, and to ease pain of the Gowt; It cooleth inflammations, agues, or frensies, and stayeth defluxions which cause a cough, or consumption: It is given in great paines of the head, and to stop fluxes of the belly, and womens courses. It is put into Mithridate, Treacle, and other medicines that procure rest, and ease pain."

He also relates the following story:

"I shall relate what I have heard of an empericall practitioner, who (being ill and not taking rest) sent to one (either Physician or Apothecary) for some Opium, when the messenger had it, the party he had it of said, There is too much for once, but I hope your Master knows that the messenger brought it home, and this emperick (it seems) took it all, and wrote to this effect on a piece of paper, I shall sleep for many hours and then wake, but forgot to give any notice thereof, after he had took it, he fell into such a sleep, that he was given over for dead, laid forth and buried; so soon as he was buried, his wife (thinking to finde some money) looking in his chamber found this writing before mentioned, whereupon she sent and had the grave digg'd up, and the coffin opened, where they saw he had turned himself when he waked."

Of mercury, after relating a case of an apothecary who accidentally drank a glass of mercury and had the blood of his heart congealed, he says:

"Others say it is a safe Medicine, & may be taken inwardly without any danger. In a word, tis good, tis bad, it cures, it kills, according as tis used; therefore I advise the vulgar not to meddle too much with it, for it hath mastered mighty Giants, and fool'd the best Artists."

Of milk, he writes:

"Milk doth nourish the body well, breeds good blood, and is very usefull in Consumptions and Ulcers of the Lungs, yea no remedy is found like it for the same: it is excellent in the bloody flux, or any other flux of the body, where there is no Feaver, nor choller abounding. It mundifieth and cleanseth, taketh away paines of the Breast, Lungs, Reines, Bladder and Entrailes, and very profitable in Ulcers of the bladder. It is good for temperate bodies, whose stomachs are free from chollerick and flegmatick humours, for in such it is well digested and engendereth good blood, and maketh the countenance faire: it asswageth heate and scalding of the urine, furthereth Venus, and is very good in times of infection."

The second part of the book on simples was printed by F. Legatt for Philemon Stephens, at the "guilded Lion in Paul's Church-yard." Mr. Stephens, it will be noted, was a careless speller. This half had the following title page:

TRACTATUS,
De facultatibus Simplicium,
The Second Part of the
TREATISE
Of the Nature and Qualitie of such Physical Simples as are most frequently used in
MEDICINES
Methodically handled for the benefit of those that understand not the Latine Tongue,
To which is added many Compound Medicines for many diseases incident to Mankind; as also an Alphabetical Table at the latter end very necessary for the
READER.

For scurvy Pemell recommends the scurvy-grasse, the name of cochlearia or spoon wort. He also says that

"Water cresses are good against the scurvie and to cleanse the blood and humours."

He gives eight other simples for the same disease and apparently did not know that any of the green things would have answered just as well.

The make-up of Pemell's book, with its table of remedies and its table of diseases with the remedies advised, is most modern. One is amused to know that he gives fourteen remedies for mad dog bites, fifty-two for dropsy, forty-five for epilepsy, and to provoke courses, sixty-four, this last doubtless as troublesome in those days as at present. A very popular present-day book on therapeutics does not mention rabies; gives twenty-two drugs for dropsy, thirty-three for epilepsy, and only eighteen for amenorrhea. This drop

in figures for the last named doubtless shows the superiority of modern surgery rather than of morals, for remember Pemell's day anticipated those of good King Charlie.

Pemell has one advantage, perhaps, and that is that most of his simples were at least harmless. Taken all in all, his is one of the least objectionable of such books and is free from the therapeutic horrors of the time.

The chief interest in Pemell is in his contribution to pediatrics. It is valuable as are all the early books on this subject, inasmuch as we glean something of the manner of practice of the earlier days and also that they act as a sort of bridge or, perhaps better, stepping-stones on which we pass from decade to decade, or from century to century. Like the immortal bard, Pemell is careless in the spelling of his name as well as other words, one of the mannerisms of the time. His books were issued by Stephens at the guilded Lion, at the guilded Lyon, and at the gilded Lyon. The title page of his pediatric contribution is as follows:

DE MORBIS PUERORUM,
or, A
TREATISE
Of the Diseases of Children;
With Their Causes, Signs, Prognosticks, and Cures, for the benefit of such as do not understand the Latine Tongue, and very useful for all such as are House-keepers, and have Children.
With the Contents of several Chapters, as also an Alphabetical Table of all the Diseases mentioned herein.
By Robert Pemell, Practitioner in Physick, at Cranebrooke in Kent. May the 29, 1653.
LONDON,
Printed by J. Legatt, for Philemon Stephens, at the guilded Lion in Paul's Church-yard. 1653.

It is a small book of 58 pages, divided into 28 chapters as follows:

THE CONTENTS OF THE SEVERAL CHAPTERS

Of Ulcers and sores in children's heads
Of Lice
Of the Scab and Itch
Of the falling Sicknesse and Convulsion
Of pain in the ears, with inflammation
Of breeding and coming of Teeth
Of inflammation of the mouth and throat, with ulcers and sore thereof
Of Feavers
Of the small Pox and Measles
Of watching out of measure and want of rest
Of fear, starting and terrible Dreams
Of Rheume, the cough, and shortnesse of breath
Of Vomiting, and weaknesse of the stomach
Of the Hicket
Of the Consumption, or leannesse, and of the Rickets
Of Gripings and fretings in the belly
Of looseness and flux of the belly
Of costiveness and stopping of the belly
Of Worms
Of Ruptures and Burstings
Of swelling, or coming forth of the Navel
Of inflammation of the Navel
Of the swelling of the Cods
Of falling of the Fundament
Of the stone, and difficulty of making water
Of Pissing in bed
Of the diseases called Saint Anthonies fire, or wilde fire, as also of burning and scalding
Of fretting, chafing, or galling of the skin in the groines

For ulcers and sores in children's heads he recommends:

"First, let the child's head be bathed with a decoction of Mallows, and Barly, or with a decoction of Dock roots, mallows, Celendine the greater, Wormwood, Fenegreek, Cicers, Lupines, Beans, &c. If there be need of greater cleansing, you may boyl the foregoing herbs in wine; or make a Lotion with decoction of Marshmallow roots, made with Urine of the infant alone, or mixt with barley water. Then anoint the head with oyl of Roses and oyl of bitter Almonds mixed with a little litharge of gold or silver in fine powder; or take of the juyce of Beets and Celendine the greater of each one ounce, Hogsgrease two ounces; boyl them together a while, then being almost cold put in of Brimstone in powder a drachme, make an ointment, with which anoint the parts affected morning and evening. Or wash the head with sope-suds made strong. If these ulcers eat to the skul, then use hony of Roses mixed with a little spirit of Wine, and afterwards the powder Birthwort and natural Balsam."

With the exception of the use of urine, which crops up in the therapeutics of all ages, even to the present enlightened period (sic), the remedies are sound for the most part. In the first place, the bath was the thing; if that did not cleanse, he added wine, the antiseptic action of dilute alcohol, only he did not have to add phenol or bichlorid or other objectionable poison, as he lived in an era before the oligarchy of Westerville had become all-powerful. Silver in fine powder finds its counterpart in the silver foil of modern surgical dressings. The action of sulphur in suppurating skin diseases is well known and is part of the Hunterian dictum that there are some skin diseases that mercury will cure, some that sulphur will cure, and some the Devil himself can not cure.

He had curious ideas about the origin of lice, which he declares "is a foul and filthy disease." His therapeutic sugges-

tions are various, but he closes with the following paragraph of sound advice:

"A powder good and safe for lice in the head.

"Take of Coculus Indy a quarter of an ounce, white Pepper a drachme; beat them into a grosse powder, and strew it into the heads of children, for it will soon destroy the lice. Or you may dip a comb in strong Mercury water, or water made with Arsenick, and so comb the childs head therewith."

As might be imagined, he had some suggestions to make on the subject of epilepsy, and they are about as satisfactory as the latest work on the therapeutics of this disease.

For teething, he recommends the following:

"Let the gums be often rubbed with the finger wet with Hony, or with Hony and Butter mixed together, or with the brains of a Hare; or the brains of a Hare mixed with Capons grease and Hony. If you can not get Hare's brains, take Conies brains.

"Rub the gums often with red Coral. It is good also to wash the outside of the cheek with a decoction of Mallows and Camomil flowers; or to anoint the same with the juyce of Mallows and Butter mixed together.

"If there be an inflammation of the gums, and the pain be very extreme, use oyl of Roses with the juyce of Nightshade.

"If these medicines prevail not, as many times comes to passe, then the best way is to cut the gums; for this is very safe, and were it more used, fewer Children would die; for I am confident the want hereof doth occasion the death of many a child."

In his consideration of measles and smallpox, he employs the usual absurd remedies of his day, but his suggestions have the great merit that if they did not help they did not hurt. He gives this sound advice about the temperature:

"You must not keep the childe too hot nor too cold, for being kept too hot it may cause faintings and swoonings, and being kept too cold, it may drive them in again, and so check and hinder nature from expelling them out to the skin."

One chapter in toto will suffice to give one a good idea of the scope and style of the book. The one on hiccough is chosen partly on account of its brevity:

CHAPTER 15—OF THE HICKET

THE CAUSE

The Hicket in Children is caused from the corrupt nourishment in the stomach, or from abundance of milk in the stomach, or from the coldnesse of the stomach by the outward air.

THE PROGNOSTICKS

The Hicket in children most times is void of danger, and the same being taken away, it doth soon cease. But if it happen to continue long, or be complicated with some other disease, as the Falling Sicknesse, or Convulsions, many times it proves deadly.

THE CURE

If the Hicket come from corrupt nourishment, or fulnesse of the stomach, 'tis good to make the child vomit either by putting your finger in the throat of it, or by putting down a feather anointed with oyl, or by some other light and easie means, that hereby the offensive matter may be taken away; then use means to heat and strengthen the stomach as in the 13. Chapter, and let the child be sparing in sucking and eating.

"If it proceed from corruption and fault of the milk, then means must be used to amend the same by good dyet of the Nurse as before, and the corrupt milk to be purged away by syrupe of Roses, or hony of Roses solutive, then to use Conserve of red Roses with red Coral in powder, or Bole-atmoniack.

"If it come from cold, then let the stomach be warmed both with inward and outward means. Give the child sirup of Mints, or sirup of Betony, and let the stomach be bathed with a decoction made of Mints, Organy Wormwood & Cyperus roots; afterward anoint the stomach with oyl of Dil, oyl of Mastick, or oyl of Mints; or apply a Pultis made with Mints and Dill seed bruised, and oyl of Mastick. Or,

Apply Mastic and Frankincence in powder (mixed with the white of an egg) to the hole of the stomach.

Or take of Mastick one ounce, Frankincense, Dill seed, ana ℥ ii, make them into powder, and mix them with the juice of Mints, then wet Hempen clouts therein, and apply it to the stomach warm."

He hit, perhaps unconsciously, upon the present-day idea of infantile diarrhea when he stated that "The cause hereof (of looseness and flux of the belly) is bad concoction, or corruption of the milk or nourishment." He continues further on:

"Sometimes when children do not breed teeth, the cause may be from the outward air, whereby the stomach & belly of the child are too much cooled, and thereby concoction is hindered; or when the stomach is oppressed with too much food or nourishment whereby crudities and corruption of the food doth follow, so that if the same be not rejected or cast up by vomiting, it is carried down to the belly and causeth these fluxes: or it may arise from bad nourishment, or from the badnes of the milk, from whence corrupt juyce is bred in the stomach which nature expels by stool. Sometimes it may proceed from the moistnes and loosenes of the bowels, which moisture hath it original from some sharp humours in the stomach, and from thence falls down into the bowels."

The above is very sound and essentially the teaching of today, although phrased differently. Incidentally he knew, as did the ancients, that a diarrhea should not be checked too suddenly.

"If the flux in children be not violent, the

danger is not great, neither must it be suddenly stopped, because the corrupt humours in the stomach hereby are evacuated or purged, which if they were stopt would prove dangerous."

He follows this with sound advice:

"If the Infant suck or not, and the flux be of some continuance, means must be used to stay it, and such means as first cleanse and then bind the body, as sirup of Roses solutive, or hony of Roses solutive. Clysters may be used."

The danger of milk in certain forms of diarrhea was noted, perhaps a little vaguely:

"Some commend the maw of a Kid, or Hare, if ten grains thereof be given, and the child to take no milk that day, least it curdle in the stomach; but give it bread boyled in water with Rosewater and Sugar."

The chapter on worms is most interesting, but is too long to reproduce here. The first part will suffice:

"Among all the diseases that are incident to children, this of Worms is not the least. There are three sorts of wormes, round, flat, and small worms called Ascharides, and are bred in the fundament.

THE CAUSE

"Worms are caused of a crude and putrified flegme and other ill humours, but never of Choller or Melancholy. For all bitter things kill worms. All manner of fruits also breed worms, especially in children and moist bodies.

SIGNS OF LONG AND ROUND WORMS

"The signs of long and round worms are these; The mouth aboundeth with moisture, the breath stinketh: terrible and fearsome dreams follow, and they gnash and grind their teeth in their sleep, and start suddenly in their sleep, their tongues are hot and dry, and they often rub their noses; they have a dry cough, and sometimes vomiting and the Hicket followeth: they feed much sometimes, and sometimes little; great drought doth most times accompany wormes, the belly is hard and swollen, and sometimes bound, but most times loose. The urine is most times white and thick, and great gripings of the belly doth follow, especially when the belly is empty. The body waxeth lean for want of that nourishment which the worms consume. Oftimes they have cold sweats, the face is sometimes red, and sometimes pale, and many times they are taken with Convulsions, and fevers happen. The pulse is very uncertain. But the most certain sign of all is, when they void worms in their excrements."

Pemell indulges in various vagaries regarding external applications, an error not entirely confined to those of earlier days and the vulgar. For example, he recommends:

OUTWARD MEANS TO KILL WORMS

"Outward means are to be used also; as you may boyl Wormwood and Centory, Peach leaves and Lupins in water, and apply them warm to the belly, or apply Cumin feed with Ox gall, or Bulls gall, or anoint the belly with the oyl of Savin, or oyl of Rue, morning and evening, warm."

Now and then Pemell forsakes his simples and wanders forth into the realms of the pharmocopœia so popular in his time. Fortunately, he does not do this often. A specimen of a prescription for incontinence of urine is as follows:

"Take a Hogs bladder, or Bores, or sheeps bladder dryed, the stones of a Hare, and the Wesand of a Cock dryed, of each half a drachme, Acorn cups two scruples, Nep and Mace, of each a scruple; make all into powder, and give hereof a scruple, or half a drachme in the distilled water of Oaken leaves; or give ten grains, or a scruple of Acorn cups in powder, morning and evening in Plantain, or Oaken leafe water."

Of course such suggestions provoke a smile, and yet in four hundred years from now there may be some who will laugh at some of our present-day therapeutics. These things are no worse than the desiccated glands as advertised and written about, witness the modern articles on endocrinology, the numerous serums and vaccines, but few of which will last an hundred, much less four hundred years.

Pemell also wrote a book called "Help for the Poor," a popular treatise on disease, its cure and prevention, but a copy of this book is not to be found in any of the larger libraries of this country. It places him forever among the front of the welfare workers as it dealt with affections most common among the indigent. It concerned the diseases of children in particular and this also places him among the pioneers of the prevention of disease and death among the young. Unheard of, almost entirely forgot, he was in his time a power for good and for progress. Just how much he influenced his contemporaries and successors it is difficult to judge, for if he had a following they did not herald his name as one who led them. In a fairly extensive reading of the earlier pediatric literature, his name has not been met with; yet he must have wielded a considerable influence.

Such is the history and work of Robert Pemell as far as one can give it today. An author of merit, a clinician of ability, a pediatric thinker in some ways ahead of his time, and one of the early workers in the field of infant welfare, his memory deserves to be kept green.

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*Dr. SEALE HARRIS, Editor
Dr. M. Y. DABNEY, Acting Editor
Dr. J. R. GARBER, Associate Editor
C. P. LORANZ, Business Manager

*Lieutenant-Colonel, Medical Corps, U. S. Army, on active duty. Granted leave of absence for period of war.

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EDITORIAL DEPARTMENT

SIR WILLIAM OSLER

Modern medical history does not record the name of a man who has accomplished more for the advancement of scientific medicine than Sir William Osler. His influence is repsonsible for much of the progress in clinical medicine that has brought the medical profession of the United States to the place where it ranks second to that of no other nation in the world.

The name and fame of Osler will ever be linked with the achievements of Pasteur, Lannaec, and Virchow; and his contributions to medical science are as great as any of them, because he popularized and applied to the bedside study of disease the principles which they discovered. It was the correllation and the practical use of the known facts regarding bacteriology, pathology, and physical diagnosis that caused Osler, and those who followed him, to be able to visualize, and therefore treat rationally, the conditions responsible for the symptoms of disease. In this plan of handling medical cases empirical therapeutics has no place, and mankind is much the gainer in being relieved from the polypharmacy that was practiced up till two or three decades ago.

For a quarter of a century Osler was the outstanding figure in American medicine, and every utterance, or written word, from him received attention as coming from one whose ability and attainments proclaimed him an authority. His opinions, therefore, have been respected perhaps as have those of no other medical man who has lived in America. He has the faculty of saying and writing things that move men to greater and nobler efforts, and none of the thousands who have known and have followed him has failed to be impressed with his wisdom and sincerity.

As a teacher Osler's peer has not been seen within the memory of physicians now living, and the methods of bedside instruction which he inaugurated in the Johns Hopkins have been adopted by all the Class "A" medical schools in the country. Osler was the pioneer in abandoning didactic lectures for group ward instruction of medical students. As a clinician, Osler has not been excelled, and his opinion was final as to the diagnosis and treatment of any case of importance that could be brought to him so long as he remained in Baltimore.

One of his former students,* writing of him, says:

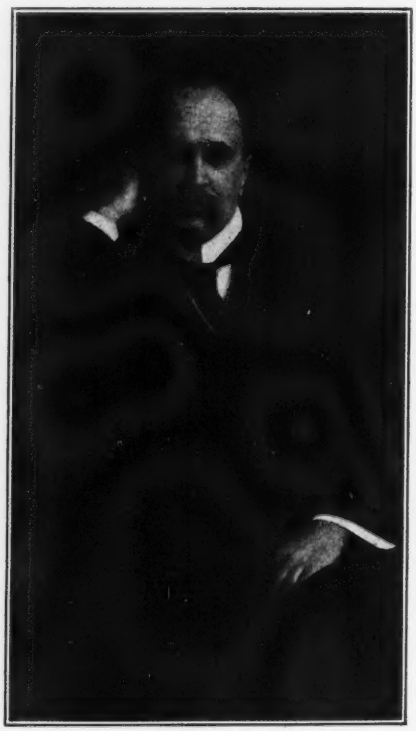
"Every one who has come into personal contact with 'the Chief,' as the Johns Hopkins men called Dr. Osler during the years he spent with us, loved him as a great teacher and physician. His former students will always remember with pleasure and pride those Saturday evening sessions when the medical group of the senior class would meet at his house and, sitting around his dining room table, would discuss with him the points of interest in the cases they had seen during the week just passed. He was such an approachable man and so human that we would forget how great a man he really was. There was no 'stand-offishness' about him as is so often encountered with many men who have reached the top of their profession.

"The point which Dr. Osler always tried to emphasize to his students was that a thorough knowledge of pathology was the *sine qua non* of diagnostic ability. He was a pathologist before he was a diagnostician and without the wonderful experience he had had as a pathologist he would have never been the diagnostician he was."

*Dr. Arthur H. Kimball, Washington, D. C., personal communication.

In addition to being a great teacher and clinician, Sir William Osler has made many valuable contributions to medical literature. Perhaps no book that has been written has had a more beneficent and far-reaching effect on scientific medicine than "Osler's Practice." Having been revised from time to time, this book is today, as it has been for more than a quarter of a century, the standard text book on medicine in many countries and has been translated into a half dozen or more languages.

Dr. Osler's many contributions to medical journals and the books on medicine which he has written have always been timely and of a very varied nature, and they have made a profound impression upon medical thought of the past three or four decades. No less brilliant, however, than his literary contributions to medicine, have been his gifts to philosophic and general literature. His "Equinimitas," "An Alabama Student" and other essays contain many gems of thought and expression that have delighted, and have influenced the lives of, many thousands of physicians.



SIR WILLIAM OSLER

When Dr. Osler was called to the Regius Professorship of Oxford University, he was accorded the highest honor that can be given to a medical man in the entire realm of Great Britain. Later he was knighted by King Edward; and, what is more, he is the recognized leader among the medical men of Great Britain. Sir William Osler has not only accomplished much in upbuilding the science and practice of medicine; he has been interested in many activities that look toward the improvement of public health conditions both in the United States and in England. To him, more than to any other one man, is due the educated public opinion which has resulted in a Ministry of Health for Great Britain.

Sir William Osler, according to regulations, is over military age—but he is still a youngster when it comes to work and achievement. He has made a number of contributions to the medical literature of the war that have been of great value, among which may be mentioned "Science and War." He has also been at the head of the medical service of a hospital for soldiers in Oxford and has given up his time to war work.

Age has dealt kindly with Sir William, since he looks the same, — a trifle older, perhaps, — as when he was "the observed of all observers" in American medicine. There is the shadow of sorrow on his face, for he has felt the sacrifice of his only son, who sleeps "in Flanders fields" with thousands of others of the finest of Britain's young manhood who "died that others might live." It seems unfortunate that Sir William's mantle could not fall upon his son, yet a man in a long life of effort could not give more to the world than did this noble youth who fought and

made the supreme sacrifice in the conquest of Germany.

Sir William's interest in, and his affection for, American physicians is as keen today as when he was in Baltimore. Any American physician is a welcomed visitor to Sir William Osler and he stands ready always to help his friends from across the Atlantic. An incident that occurred during the recent war illustrates his influence in England and exemplifies his generosity and his interest in American medical effort.

In May of 1918 the Commission on Trench Fever of the American Red Cross, in France, had completed its investigations and was ready with its report, which would make up a book of between 400 and 500 pages. The paper for publishing this valuable report could not be procured in France, and the effort to have it published in London failed. Sir William Osler was appealed to, and in a five minutes' conversation with the manager of the Oxford Press he had arranged for the publication of the "Trench Fever Report." The Oxford Press had agreed to publish other books pertaining to war medicine and surgery, but Sir William's appeal that the "Trench Fever Report" was of most importance, and that "we should show this courtesy to the medical profession of the United States," accomplished what could not be done by others in Paris and London.

Baltimore being a Southern city, all of its institutions are regarded as a part of the South, as well as of the Nation; and so long as Dr. Osler remained in Baltimore, 'though he retained his citizenship in Canada, he was claimed as a Southerner. In his courtesy and kindness to all with whom he came in contact, he surely had the characteristics of a Southern gentleman. His influence on the advancement of medicine in the South can not be over-estimated and, in honor of his seventieth birthday, it seems only fitting that the SOUTHERN MEDICAL JOURNAL should publish an "Osler Number," made up of contributions of his Baltimore confreres and his former students.

At seventy years of age Sir William Osler is recognized as the Nestor of Anglo-Saxon medicine, and he is today the most honored and the best beloved medical man in all the world. The entire medical profession of the South joins with the JOURNAL in felicitations to this remarkable man. It is the wish of all that his health, happiness, and usefulness may continue until he can look back over a century of years that have been spent in great attainments.

MILK-BORNE INFECTIONS

Since milk is a good culture medium for many pathogenic bacteria, and the way in which it is handled, renders it very easy of contamination, this important article of food is frequently infected. Milk, therefore, is the source of many acute illnesses, particularly during the summer months.

The pathogenic micro-organisms that are carried by milk may be derived from animals infected with bovine disease. Cows may have diarrhea due to the *Bacillus enteritidis*, the organism responsible for many outbreaks of food poisoning. This bacillus may pass from the blood stream, through the milk ducts into the milk of an infected cow, or it may come from the feces which gets on the udders and from there pass into the milk. Cows are also known to have been infected with paratyphoid bacilli and they may be "carriers" of the *Bacillus enteritidis*, the *Bacillus paratyphosus* and other bacteria that are pathogenic to human beings. The milk from animals which have puerperal or other forms of septicemias, and that from cows having local streptococcic or

staphylococcic infections of the udder may also produce gastro-enteritis in adults as well as in children. Cows may also be afflicted with, and through their milk they may transmit, tuberculosis, anthrax, foot and mouth disease, actinomycosis, and other diseases that infect man and animals.

Milk, however, is most frequently infected from outside sources; and the human carriers of the *B. coli, B. typhosis, B. paratyphosus, B. enteritidis, B. dysenteriae, streptococcus, B. enteritidis,* and other micro-organisms are generally responsible for the infection of milk. In the summer diarrheas of infants and the outbreaks of bacillary dysentery among adults, the infection is usually of one of the above types. Milk is also the vehicle for carrying other infections to man. Among these are scarlet fever, diphtheria, and streptococcic sore throat. Flies, dust, unclean milk vessels, and unclean hands of the milker and others who handle milk and its products are the usual sources of infection.

Milk that is fresh from the cow, if properly handled as is done by certified milk producers, contains very few micro-organisms, and if kept cold will be pure and wholesome for days; whereas, milk that is handled by dirty and careless milkers, and placed in unclean vessels, and is not kept cold, becomes seething with bacteria in a few hours; and if pathogenic micro-organisms happen to be present, it is therefore poisonous to the consumer. Milk infections are much more frequent in summer than in winter for the reason that the pathogenic bacteria propagate best in warm weather.

The majority of cases of milk infections are mild, having only the symptoms of an acute gastro-enteritis, i. e., nausea, vomiting, abdominal pain, and diarrhea. Sometimes, however, particularly with infants, there is a high degree of toxemia characterized by high fever, convulsions, or stupor, coma, and death.

It should be remembered that the same milk which causes the acute symptoms of food poisoning may also be infected with the organisms of typhoid or paratyphoid fevers, and that after the acute symptoms subside the patient may develop a more or less typical attack of one of those diseases. Bacteriological studies of the blood, urine and feces, and the agglutinin reactions of the blood serum of the patient may reveal the type of infection.

IMPURE ICE CREAM

Many outbreaks of poisoning have been traced to eating ice cream. It was formerly thought that tyrotoxicon formed in ice cream which was allowed to melt and was kept in tin freezers was the active toxic principle in ice cream poisoning. But it is now known that the toxic symptoms that follow the use of impure ice cream are due to the bacteria which contaminate milk. Freezing does not destroy the colon and allied group of organisms that pollute milk, and since the milk that is used in the manufacture of ice cream is sweetened and flavored, it is often not kept so carefully as is milk that is sold for drinking purposes. Ice cream, therefore, can be made of milk that is not clean nor fresh, and is likely to contain a large number of bacteria, with concentrated toxins.

Many outbreaks of typhoid and paratyphoid fevers have been traced to eating ice cream. One such epidemic that occurred in Birmingham, Alabama, in 1915, was thoroughly studied by Dr. L. L. Lumsden, of the United States Public Health Service. In this epidemic there were more than 1,000 cases, many of which gave a history of having eaten ice cream. On inquiry it was found that a large number had purchased the ice cream from retailers who patronized one large wholesale

ice cream establishment. Outbreaks of typhoid also occurred in several towns near Birmingham among the customers of retail dealers who purchased ice cream from the Birmingham manufacturer. An investigation of the ice cream plant and the source of its milk supply proved unmistakably that the source of infection in more than 1,000 cases of typhoid fever was ice cream. The epidemic subsided when this large ice cream factory was made sanitary, after having discovered an employee who was a typhoid carrier, and after the city government required ice cream dealers to pasteurize all milk used in the manufacture of ice cream.

THE PREVENTION OF MILK-BORNE INFECTIONS

The pasteurization of milk destroys most of the pathogenic bacteria and their toxins with which it may become contaminated. So well known is this fact that many cities have installed pasteurization plants in which all milk is pasteurized before it is allowed to be sold, and in many others the milk dealers are required to pasteurize their milk under the supervision of the city health department. In the cities requiring pasteurization of milk there has uniformly followed a reduction in the sickness and death rates from typhoid fever and infantile diseases.

It is possible, and even likely, that milk may become infected before it reaches the consumer, even after it has been pasteurized by the milk dealers. It is, therefore, best, particularly in hot weather, to pasteurize the milk at home before it is used. Pasteurization is said to destroy some of the vitamins in milk, but they can be supplied to babies in fruit juices and to older children and adults in fruits and vegetables. It is better to risk nutritional disorders than to have infections that so frequently follow the use of raw milk, particularly in the warm months of spring, summer, and autumn.

It is as necessary for public health authorities to inspect and regulate the sale of milk that is sold for making ice cream as that intended for drinking purposes. Every soda fount, and every place where milk or ice cream is sold, either by retail or wholesale, should undergo rigid inspection. This is carried out to some extent in the cities, and it has been found in a number of places where ice cream dealers have been required to pasteurize the milk used in the manufacture of ice cream that the typhoid rate has been materially reduced. It is just as important in small towns as in cities to pasteurize the milk used for making ice cream. Milk is regarded as an essential article of nourishment for children, and properly handled is an ideal food; but "eternal vigilance" on the part of those who handle milk is necessary to prevent its becoming extremely dangerous for human consumption.

THE MEDICAL AFTERMATH OF WAR*

The American people appreciate the unselfish spirit that prompted so many of the best men in medicine and surgery to give up the comforts of home, the joy of family and friends, and the emoluments of an established clientele, to serve their country in the greatest crisis in history. The 30,000 doctors who entered the Army may be poorer in purse when they return to their homes, but they will be rich in experiences that will be of the utmost help to them in their daily work. The medical profession is therefore coming out of the war the most respected of the learned vocations.

Aside from the prestige that will come

*War Medicine, January, 1919.

to the doctors who served as military officers, they will be better men and better physicians through having been associated with others in their profession as they have in army life. It happens only too often that medical men in villages and cities, if they are fortunate, develop an "overweening" conceit because of their success, while the less favored sometimes come to think that the physician or surgeon who builds up a good practice does so by employing unprofessional tactics. Then there is the jealousy of the successful ones among each other, and in the cliques that surround them in every city. There will be less of envy and jealousy and a more tolerant spirit among physicians and surgeons as a result of the war than ever before, because they have been associated with so many men who they know have worked unselfishly, and they have had the intimate contact with their professional brothers that broadens thought, and makes men act with greater kindness and generosity toward one another.

COMMUNITY HOSPITALS

Medical men, particularly in small communities, have suffered from the lack of co-operation. There may be in a town four, five, eight or ten good doctors, one or two of whom have had good surgical training; another may be a good diagnostician, while another is better fitted for laboratory work. But because they have not pulled together, none of them has done the thorough scientific work of which he is capable. As a result, in times past, when their good-paying patrons needed expert medical and surgical advice, they have been sent to the cities for diagnosis and treatment. The medical men who have served in the Army have seen as good surgery in tents, shacks, or in residences converted into temporary hospitals, as they have in the finest surgical amphitheater in the great medical centers. They have not only seen as good work done, but many who never had the opportunity of doing surgery before have been trained in surgical technic by association with the masters in surgery who have been in France, and have learned that they can perform many of the major operations with as good results as their teachers.

When these men go home, they will associate themselves in clinical groups; they will build up and equip inexpensive hospitals; they will take post-graduate courses in the line of work in which they are best prepared to specialize; and they will be prepared to give their patients as good medical and surgical attention as they could get in the larger cities. They will be more thorough and accurate in their work. For instance, the diagnosis of appendicitis will be made earlier and operated upon in the village hospital without submitting the acute appendix cases to the dangers of delay and travel that have cost many a life.

TEAM WORK

The constant association with each other of internists, surgeons, roentgenologists, bacteriologists, pathologists and medical men in other lines, in the thorough work that has been done, particularly in the base hospitals, will make men engaged in practicing all branches of medicine desire to give their patients at home the same attention. Consequently, they will arrange to be associated with similar groups of specialists when they begin private work again. They will realize that general practitioners in the future, more than ever before, will refer their cases to men who can give them the benefit of such group consultations.

The general practitioner, the keystone of the arch upon which the whole founda-

tion of medicine rests, is coming out of the World War bigger, broader and more resourceful than ever before. In the past he has been overworked, and only too often did not have the time to study his cases thoroughly, and for that reason has not been so accurate in his diagnoses as he should have been. In many instances, he has not availed himself of the advantages of the laboratory. In army work he has had the opportunity as never before of seeing cases studied with the aid of the laboratory and the x-ray, and with the co-operation of dentists, ophthalmologists, neurologists, urologists and other specialists. When he returns home, he will see to it that his patients receive the benefit of the aids in diagnosis and treatment to which he has become accustomed in army work.

Laboratory and x-ray men have also profited by their association with general practitioners, internists and surgeons, and they will not be so "cocksure" of their diagnoses without clinical assistance. In other words, medical men have learned the advantages of, and necessity for, team work, that will be carried into their private work, and their patients will profit thereby, while they themselvves will also be gainers by co-operating with their medical confreres.

THE SURGEONS

The great surgeons of the United States, and the best men in all branches of medicine, with few exceptions — and most of those who did not ask for commissions were over-age or had physical disabilities—volunteered their services for army work; and they have given the best that was in them in treating our sick and wounded soldiers. Indeed, there has been no finer spirit of patriotism manifested than that of the surgeons of the United States, who in many instances closed up their private hospitals and gave up incomes amounting to many times the salary of a major, the highest commission in the Army to which a Medical Reserve Corps officer could attain in the first year of the war, and asked for nothing except the opportunity to give their services to the men who were to fight their country's battles. And the surgeons have served faithfully and well; but, while serving, they, too, have profited by their army work. The contact with others has broadened their viewpoints, and they have had experiences, particularly in bone and emergency surgery, which will be helpful to them in their work at home.

A prominent surgeon said that one of the great things that has accrued to surgery from the war has been the more general use of nitrous oxid and oxygen anesthesia, which, if given properly (usually three-fourth nitrous oxid to one-fourth oxygen), actually raises blood-pressure and prevents or lessens shock, thereby decreasing the danger of surgical anesthesia. He also said that the advent of the trained female anesthetist is one of the permanent benefits to surgery that has come from the war.

The leaders in surgery have discovered many first-class surgeons of whom they had never heard before; and they have been frank enough to admit that the best surgeons are not all working in the great surgical centers, but that there are many good operators in obscure parts of the country. There will always be men who, because of great achievement, will be recognized as leaders of their profession, but the war has been a great leveler of surgeons as well as of men in other lines of work. It has developed the latent talents of many well-trained men, who after the war will take their places as among the most competent surgeons of the century.

It is no doubt true that the Army will

turn out some "half-baked" surgeons who will develop the *furor operativus* and be a menace to their communities; but it will not take their patrons long to learn that with the surgical tyro "the path of glory leads but to the grave" and amateur surgery will prove unprofitable and fall into deserved disrepute.

THE IMPETUS TO RESEARCH WORK

American laboratory workers were not in the war long enough to accomplish a great deal in medical research, 'though the original studies and investigations, notably on trench fever, have made important contributions to the science of medicine and surgery. A number of surgical problems were being invvestigated in France on a large scale when the war closed. There can be no question, however, that the war has stimulated research work on many lines and that it will be continued in the laboratories of the United States as well as in those of our Allies. The public has received some needed education in the importance of research work on many lines, and it will be easier to induce legislators and philanthropists to provide funds to establish new research laboratories and to develop those that already are doing such good work. The contact with the research men of Great Britain and France has stimulated our men to greater efforts; and we have learned from them that it is duty of Government to provide greater facilities for laboratory and research work, and appropriations for such purposes will be easier to obtain in the future.

VENEREAL DISEASES

The war has brought to the attention of the public the fact that venereal diseases are among the greatest public health problems. Actual demonstrations have been made, which have proved to the satisfaction of all unprejudiced men that houses of prostitution are centers of infection that cannot be tolerated, and public officials in every city in the United States will be forced to regard organized vice as a health problem. As a result of the war the United States Government has appropriated $1,000,000 to be allotted proportionately to the various states, provided they add an amount equal to that given them for work in preventing venereal diseases. When American physicians return home, they will find genito-urinary dispensaries and prophylactic stations everywhere.

The public will understand, better than ever before, the necessity for the accurate diagnosis, and the thorough and scientific treatment of gonorrhea and syphilis, with their complications and sequelæ; and though there will be a decrease in venereal diseases, the urologists will be busier than ever before. The specialty of urology will, therefore, attract many men now in general practice, and it will become of greater importance than ever before.

PREVENTIVE MEDICINE

There have not been many important advances made in the methods of preventing disease as a result of the war, but an impetus has been given to public health work that will last long after the soldiers have returned to their homes. More than 3,000,000 citizens of the United States have been taught something about military hygiene, which differs but little from that of civil life. They will go back to their homes where they have tolerated many sanitary crimes because they did not know better. They will not only live more hygienic lives themselves, but they will see to it that their neighbors do not harbor infection on their premises. Doctors from civil life have learned much about preventive medicine, which on their return to civil practice they will employ in private work. Then the Army has trained a large number of sanitarians who will be avail-

able for public health work after the war.

The epidemics that have occurred incident to bringing together large bodies of men, and the fact that approximately twenty-five per cent. of the young men of our country are not fitted for military service because of physical disabilities, have taught the public the importance of preventive medicine. The draft law also brought out the necessity for accurate birth statistics, and among the aftermaths of the war may be the assurance that we shall have more reliable vital statistics. In other words, the war has helped tremendously to get an enlightened public opinion on health matters that is essential to success in carrying out methods for preventing communicable diseases, and as a result Congress will not delay much longer the needed legislation providing for a National Department of Health with a sanitation in the President's Cabinet.

All of the advances in the science and practice of surgery resulting from the war cannot be questioned in an editorial comment. There is no question, however, that mankind has been and will be the gainer by the efforts of American physicians who have sacrificed to serve.

Southern Medical News

ALABAMA

Dr. W. O. Owen, Colonel, M.C., addressed the Jefferson County Medical Society at a recent meeting on "Lessons in Medicine and Surgery Learned from the War."

At a meeting of the Board of Trustees of the Alabama Insane Hospital on July 1 Dr. Wm. M. Faulk, Tuscaloosa, was elected to the position of Assistant Superintendent of the Alabama-Bryce Insane Hospital. Dr. Faulk will assist Dr. W. D. Partlow, who has been made Superintendent of that institution.

Dr. S. W. Welch, State Health Officer, Montgomery, attended the meeting of the State and Provincial Health Officers of North America, called to meet with the Surgeon-General of the U. S. Public Health Service in Washington in June.

Dr. Burr Ferguson, who for a number of years practiced medicine in Birmingham, has been employed by the State Board of Health to form a part of the working force of the Board during the coming year. He will probably be in charge of the Bureau of Communicable Diseases. Dr. Ferguson recently returned from France, where he won promotion to the rank of Lieutenant-Colonel.

ARKANSAS

Dr. F. T. Isbell, Horatio, was presented with a silver loving cup by his associates on the Arkansas State Board of Examiners upon the occasion of his retirement as President of the Board.

Dr. R. F. Darnall has severed his connection with the State Hospital for Nervous Diseases.

Dr. C. M. Lutterloh has recently been reappointed County Health Officer for Craighead County.

Dr. P. P. Boggan, Forrest City, has been reappointed by the State Board of Health as County Health Officer of St. Francis County.

Drs. W. F. Smith, Little Rock, and J. A. Bogart, Forrest City, have been reappointed to their offices on the State Medical Board.

The United States Public Health Service is being gradually eliminated in Little Rock, and the Little Rock Board of Health is organizing its forces to continue the work where the Government has left off. Dr. Morgan Smith is acting as Chief Health Officer by authority of the City Council. The Board of Health selected Lieutenant Harry H. Emerson for Inspector of Food, Meat and Milk, with R. T. Beard as his Assistant. Lieutenant Emerson has been working in connection with the United States Public Health Service and Mr. Beard has been serving with the Department as Sanitary Inspector.

More than 3,000,000 school children have qualified as Crusaders in the Health Campaign conducted jointly by the Junior Red Cross and the National Tuberculosis Association.

At a recent meeting of the Board of Health, Dr. G. T. Townsend, Dr. Morgan Smith and Alderman P. C. Richardson were appointed a committee to receive applications for the position of an all-time health officer to succeed Dr. Townsend, who soon is to be transferred by the Surgeon-General. It was agreed that Pulaski County and North Little Rock each would be asked to contribute $5,000, leaving Little Rock $10,000 to contribute to the continuation of the mosquito control work.

Deaths

Dr. B. V. Madole, Danville, aged 50, died at his home in June, after a lingering illness.

DISTRICT OF COLUMBIA

The meeting of the State and Provincial Health Officers of North America, called to meet with the Surgeon-General of the U. S. Public Health Service in Washington in June, was one of the best attended meetings in the history of the organization. There are forty-five states and all the provinces of Canada included in this organization, and there were forty-three states represented. The subject of public health and its difficulties was widely discussed.

FLORIDA

The University of Florida, Jacksonville, has inaugurated a plan by which a special course in community health problems will be offered during the summer months. The course began June 1 and is under the direct supervision of H. R. Hixson, Secretary of the State Anti-Tuberculosis Association.

The Duval County Medical Society has petitioned the State Legislature not to pass the bill that seeks to cut the appropriation of the State Health Department by 50 per cent.

GEORGIA

At the recent commencement of the University of Georgia the honorary degree of Doctor of Science was conferred on Dr. J. M. T. Finney, Brigadier-General, M.C., Professor of Clinical Surgery, Medical Department, Johns Hopkins University.

After serving in France for more than a year, Captain L. W. Wiggins recently received his discharge at Camp Gordon and has resumed his practice in Atlanta.

Dr. R. L. DeSaussure, Rome, was elected to succeed Dr. M. M. McCord as County Health Officer at a recent meeting of the Floyd County Board of Health. For five years Dr. DeSaussure has been a commissioned officer in the United States Public Health Service.

KENTUCKY

The Health Committee of the Woman's Club held a meeting in Louisville on May 13 for the purpose of stimulating interest in the formation of a Kentucky Public Health Association.

The Henry County Medical Society held its regular meeting during May, at which time officers were elected for 1919. Dr. O. B. Humston was chosen President; Dr. W. F. Ashbury, Vice-President; Dr. W. B. Oldham, Secretary.

Dr. W. E. Render, formerly assistant physician in Lakeland Hospital for the Insane, and now in the Medical Corps of the Army at Fort Benjamin Harrison, has accepted an offer to become Assistant to Dr. W. E. Gardner in the Louisville Neuropathic Sanatorium. Dr. Render is expecting his dicharge in a few days.

Dr. Thomas C. Holloway has been discharged from the Medical Corps of the Army and has resumed practice in Lexington.

Deaths

Dr. Junius A. Woolfolk, Owensboro, aged 63, died at his home following an injury sustained in an automobile accident.

LOUISIANA

An invitation to all persons connected with the medical profession to interest themselves in the annual meeting of the American Public Health Association in New Orleans October 27 to 30 is one of the features of the late

(Continued on page 28)

Dr. William Krauss Dr. C. R. Stingily

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PHARMACEUTICAL & BIOLOGICAL CHEMISTS
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(Continued from page 432)

issue of the Quarterly Bulletin of the Louisiana State Board of Health. The membership of the Association is composed of health officers, laboratory workers, medical inspectors, vital statisticians, sanitary engineers, social workers and physicians. Articles on malaria, birth registration, drug prohibition, child hygiene and the history of influenza are included in the Bulletin.

MARYLAND

At the recent commencement of the University of Georgia the honorary degree of Doctor of Science was conferred on Dr. J. M. T. Finney, Brigadier-General, M. C., Professor of Clinical Surgery, Medical Department, Johns Hopkins University.

Deaths

Dr. A. V. Cherbonnier, formerly of St. Louis, died at his home in Baltimore early in July.

MISSISSIPPI

The State Board of Health has appointed Dr. W. S. Cranford, Ellisville, County Health Officer of Jones County. The appointment is for a two-year term, beginning June 24, 1919.

Dr. T. R. W. Wilson, for several years Director of the Camp Shelby Base Hospital, has been chosen to succeed Dr. C. R. Stingily as Head of the Mississippi Hygienic Laboratory at Jackson.

MISSOURI

The State Tuberculosis Sanitarium, at Mount Vernon, has authorized the employment of an additional staff man for the purpose of having charge of the laboratory work.

Dr. Edwin C. White has been discharged from the Medical Corps of the Army and has resumed practice at Kansas City.

Dr. W. P. Bradley has resigned his position as Superintendent of the State Hospital for the Insane at Nevada, Mo. Dr. T. M. Craig has been appointed as his successor and Dr. Robert Bradley as his Assistant.

Dr. M. J. Armstrong, Springfield, was elected Assistant Physician and Bacteriologist at the Missouri Sanitorium, Mt. Vernon, at the monthly meeting of the Board of Managers held in June.

Dr. Cyrus D. Cantrell has received his discharge from the Army and has resumed his practice at Kansas City.

Tests of the water in natatoriums and swimming pools in St. Louis are made weekly by Assistant Health Commissioner Jordan.

Deaths

Dr. L. M. Drake, St. Joseph, died at his home following injuries received in an automobile accident.

Dr. H. W. Latham, aged 67, at Latham, died suddenly June 26, following a stroke of apoplexy.

NORTH CAROLINA

City Health Officer Garnett, Danville, has issued warning to local physicians to report more promptly the occurrence of infectious diseases.

(Continued on page 30)

Laboratories of Drs. Bunce and Landham

ATLANTA, GEORGIA

Allen H. Bunce, A.B., M.D.
Director Pathological Dept.

Jackson W. Landham, M.D.
Director X-Ray Dept.

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The X-Ray laboratory is equipped with a modern 10 Kilowatt Snook Transformer and a Single Unit Victor Table adaptable to both vertical and horizontal fluoroscopy and radiography. Both diagnostic and treatment work is done in this department personally by Dr. Landham, who was formerly associated with Dr. W. F. Manges, in Roentgenology, at the Jefferson Medical College and Hospital.

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Many Times Tissue Work and Many Other Bacteriologic Examinations are Useless

—if you don't have the examination and report of findings performed and mailed promptly.

I know how to render you this service, because I have superior facilities and use only the most modern, recognized Army methods.

These methods also assure you that a reasonable fee will be charged.

For instance,—an ordinary examination of tissue specimen is made, findings compiled and mailed post-haste upon day of receipt. Or, when requested, I can report by telegram or telephone that same day.

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TISSUE	$5.00
WASSERMANN TEST	5.00
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All other Bacteriologic service performed in proportion.

My services and laboratory facilities are always at your disposal upon command.

DR. JAMES S. FLEMING

Pathological Laboratories
Exchange Building,
MEMPHIS, TENN.

(Continued from page 28)

The Health Officer claims that the citizens are placed in an unwarranted danger of disease through failure of doctors to do their duty.

Dr. H. E. Miller has been appointed to succeed Warren Booker as Chief of the Sanitary Engineering and Inspection Bureau.

The Mecklenburg County Medical Society held its usual meeting in Charlotte during May.

OKLAHOMA

Dr. E. O. Barker has recently been elected City Physician of Guthrie.

The Rogers County Medical Society met in Claremore June 23 and adopted the following new fee schedule, which corresponds to the one used in Nowata and other adjoining counties: Day calls in city, $3.00; night calls in city, $5.00; day calls in country, $3.00 first mile and $1.00 for each additional mile one way; night calls in country, $5.00 first mile and $1.00 for each additional mile one way; obstetrics, normal case in city, $25.00; in the country, regular mileage extra.

Dr. L. T. Gooch, Lawton, has been appointed Superintendent of Health for Comanche County, succeeding his brother, Dr. E. S. Gooch.

Seven hundred doctors of a total of 2,672 in the State responded to the call to the colors of physicians during the war, according to a statement by Dr. L. Haynes Buxton, President of the Medical Section of the Oklahoma Council of Defense.

Dr. W. C. Graves, McAlester, has been appointed County Physician of Pittsburg County by Dr. A. R. Lewis, State Health Commissioner. He succeeds Dr. W. W. Sames, of Hartshorne, who resigned several months ago.

Dr. C. M. Bloss, Okemah, has been reappointed Superintendent of Health of Okfuskee County.

The State Board of Health is planning a systematic campaign of the State to administer typhoid vaccine as a precaution against the spread of typhoid fever as announced by Dr. A. R. Lewis, State Health Commissioner.

Dr. E. W. Hooper has recently been discharged from the Army service and has resumed his practice in Pawhuska.

Deaths

Dr. David G. Reece, aged 55, of Braggs, died June 19th at a hospital in Fort Smith, Ark.

TENNESSEE

The Upper Cumberland Medical Society held its annual convention in Cookeville during May.

The East Tennessee Medical Association held an interesting session in Lenoir City during May.

Dr. John Overton, Nashville, has recently been appointed Prison Physician at the main prison.

Dr. Clarence Turner, Gibson County, has succeeded Dr. V. A. Biggs, Martin, as a member of the State Board of Health. His term holds for six years.

Dr. L. D. Bristol, Commissioner of Health for the State of Maine, has accepted an appointment as Professor of Public Health in the College of Medicine, University of Tennessee. Dr. Bristol will assume his new duties August 1.

Dr. A. K. Shelton has been reappointed to the

(Continued on page 32)

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Dr. R. B. H. Gradwohl, Director

(Continued from page 30)

position of Physician at Petros Branch Prison by Governor Roberts.

Dr. J. W. Oursler, recently discharged from the United States Army, has resumed his practice at Humboldt.

Resolutions indorsing the proposed sanitary survey of Memphis supported by the City Club were passed by the members of the Memphis and Shelby County Medical Society at the regular meeting of that organization July 1. Only one meeting of the Society will be held each month during the summer. The bi-weekly meetings will be resumed in October.

Surgeon-General Blue has appointed Dr. P. B. Lusk, of Jackson, Medical Examiner for the Government in Madison County.

TEXAS

The Wharton-Jackson County Medical Society held its annual election of officers at its meeting in El Campo May 10. Dr. D. P. Redwine, El Campo, was elected President; Dr. Green Davidson, Wharton, Vice-President; Dr. S. D. Kahn, El Campo, Secretary.

The Dallas Board of Health has petitioned the Surgeon-General, U. S. Public Health Service, to permit Leslie C. Frank to take charge of the City Health Department.

Dr. C. W. Goddard, State Health Officer, announces that the health survey being carried on in Denton will be completed in a few weeks.

At a recent meeting of the El Paso County Medical Society it was voted to increase charges for professional services by 25 per cent. The new prices have been inaugurated.

Dr. Lane B. Cook, Dallas, has been appointed City Health Officer and Raymond H. Davis, City Sanitarian.

Dr. Frank H. McGregor, Temple, has been discharged from Army service and has resumed his practice.

The semi-annual session of the North Texas Medical Association met in Dallas in June. An address on sleeping sickness by Dr. K. H. Beall, Fort Worth, and discussion that followed the address was one of the features of the meeting. The next meeting will be held in Fort Worth. At the close of the meeting the following officers were elected: President, Dr. H. Leslie Moore, Dallas (elected for the eighteenth time); Vice-President, Dr. Sidney J. Wilson, Fort Worth; Secretary, Dr. David L. Bettison, Dallas; Treasurer, Dr. M. L. Wilbanks, Greenville; Counsellor, Dr. A. B. Small, Dallas.

At a recent meeting of the Orange County Medical Society at Orange every member was present.

At Atlantic City in June the Air Service Medical Association of the United States perfected a permanent organization and elected officers as follows: President, Col. John O. McReynolds, Dallas; Vice-Presidents: Col. T. C. Lyster, New York, N. Y.; Col. Eugene R. Lewis, Dubuque, Iowa; Col. I. H. Jones, Philadelphia, Pa.; Col. W. H. Wilmer, Washington, D. C.; Col. Albert

(Continued on page 34)

Safe Summer Diet for Infants

Borden's Eagle Brand—highly nutritious, readily digested and assimilated, uniform in quality and easily prepared. Offers a particularly valuable infant diet during the summer months when heat threatens the wholesomeness of fresh cow's milk.

Eminently suitable as an all-season diet for infants, Borden's Eagle Brand can be prescribed with entire confidence in its wholesomeness and freedom from contamination. Its use eliminates the danger often present in milk of unknown, unidentified origin.

Rich in nutritive value and tissue building elements and at the same time easily digested, Borden's Eagle Brand is pleasingly tolerated by delicate stomachs that many times rebel against an excess of fats.

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The oat yields 1810 calories per pound in the energy unit of food value. Round steak yields 890.

One-sixth of the oat is body-building protein.

The oat is rich in needed minerals—richer than beef.

It is almost a complete food.

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DENTAL X-RAY FILMS. Fast or slow emulsion, regular or oval shapes. Small size, 50c per dozen. Lead backed films (no sharp corners), 85c per dozen. **FILING ENVELOPES** with printed X-ray form. (For used plates).

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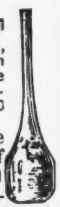

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(Continued from page 32)

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Dr. J. P. McAnulty has been discharged from the Army and has resumed practice at San Angelo.

Dr. William F. McManus has been discharged from the Army and has resumed practice at San Antonio.

Dr. Grady Shytles, Texarkana, who has been conducting a campaign in the interest of sanitation in Bowie County, reports the work in good shape.

Deaths

Dr. Leslie K. Warren, formerly of Nashville, Tenn., died the latter part of June in a hospital in El Paso, after long illness.

Dr. J. T. Rice, aged 70, died in June at a local hospital in Texarkana following a long illness.

Dr. A. A. Ledbetter, Hallettsville, aged 76, died the later part of June following an illness of several weeks.

(Continued on page 36)

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Internes Wanted—St. Joseph's Hospital (a three-hundred bed general hospital) needs two more internes, and would be glad to consider applications. Recent graduates preferred, state school graduated from, and year of graduation. Compensation, board and lodging, and instruction. Term of service, one year. Apply to Dr. O. S. McCown, Bank of Commerce & Trust Building, Memphis, Tenn., President of Staff.

The Memphis General Hospital School of Nursing offers to young women a thorough three years course of instruction, covering all diseases except smallpox, including all branches of surgery, medicine, pediatric and contagious nursing. Students are given a monthly allowance and full maintenance. Application should be made to the Superintendent of Nurses.

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FOR SALE at reasonable figure, one Scheidel-Western 10 K. V. A. X-ray Transformer, combination table for general stereoscopic and horizontal fluoroscopic work, and stereoscopic viewing stand. All in splendid condition. Address E. C. C., care SOUTHERN MEDICAL JOURNAL.

WANTED—Position as Surgical Assistant, or with Milling or Construction Company by graduate of "Class A" school; class of 1917; can do routine laboratory work; eleven months' active service in Army; married. Address J. J. S., care Southern Medical Journal, Birmingham, Ala.

A SURGEON, graduate of Class A school, 9 years' civilian practice and two years' service in the Navy, and who is at present "Chief of the Surgical Service" in a Naval Hospital that is caring for 16,000 Marines, desires a position as House Surgeon in a general hospital, or to be associated with several men interested in "Group Medicine"—he to do the Surgery. X. Y. Z., care Journal.

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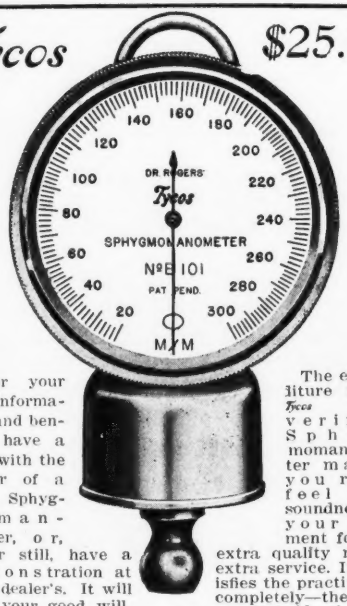

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The expenditure for a *Tycos* Self-verifying Sphygmomanometer makes you rightly feel the soundness of your judgment for the extra quality means extra service. It satisfies the practitioner completely—the reason it holds the unchanging loyalty of users.

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Arseno-Benzol			Diarsenol		
0.3 Gram	Pkg.	$1.15	0.3 Gram	Pkg.	$ .90
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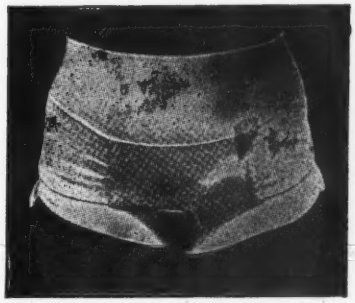

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Samples of Dennos on request. Also Dennos Prescription Pencil FREE.

Dennos Products Co.

2025 Elston Ave., Chicago, Ill.

(Continued from page 34)

Dr. D. F. Jones, Sherman, died in June from injuries received when an H. & T. C. train hit his automobile.

Dr. S. W. Rimmer, San Saba, died February 14.

VIRGINIA

Dr. H. S. Hedges, Charlottesville, who has been confined to his home for several weeks following an operation, has sufficiently recovered to resume his duties.

Cities and towns in Virginia which wish to undertake anti-malaria campaigns will be helped by the United States Public Health Service, the State Board of Health and the International Health Board. Dr. Ennion G. Williams, Health Commissioner, believes that the campaign made possible by this combination of agencies can go far toward controlling malaria in the districts that will undertake the work. The Public Health Service offers to place at the disposal of the State authorities two trained engineering experts, whose salaries and expenses will be paid entirely by the Government.

Deaths

Dr. Richard F. Taylor, aged 48, died recently at his home in Mannboro, after an illness of a week of pneumonia.

WEST VIRGINIA

Dr. Emerson Megrail, recently discharged from the Army, has opened offices in Wheeling.

Dr. J. E. Marschner, Wheeling, has been appointed City Health Officer, succeeding Dr. M. B. Williams.

NOW ENTIRELY AMERICAN

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PALATABLE and EFFICIENT IODIN MEDICATION

Especially Suitable for Prolonged Use as in

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AGREEABLE and RELIABLE URINARY ANTISEPTIC

For Acute and Chronic Cases of

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VERONAL and VERONAL-SODIUM

The Well-Known Hypnotics

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PASTEUR'S ANTI-RABIC VIRUS.

Full Course Treatment.....$25.00

as improved and made by DR. D. L. HARRIS, St. Louis, Mo. U. S. Government License 66.

The treatment is so stable that it can be shipped anywhere and kept any reasonable length of time without loss of immunizing value.

By this method a virus of constant and known potency is used and dosage can be accurately determined.

In a series of experiments made by Poor, Jelneck and Gibson, in the New York City Health Department, it was found that the injection of Harris' dried vaccine resulted in an earlier establishment of immunity than that produced by the old Pasteur method, and that the immunity was at least twice as great.

With this virus the doctor can treat the patient in his office and the patient does not have to be sent to an institution.

Telegraph orders given prompt attention.

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Accurate histological descriptions and diagnoses of tissues removed at operation should be part of the clinical record of all patients.

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$20

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Gives you guaranteed mercurial accuracy with pocket size convenience. Registers both systolic and diastolic pressures up to 300 millimeters. Neat case, 2¾ x 2¾ x 12½. Easily carried. Always ready for use. Send check for $20.00 and outfit will be delivered to your office prepaid.

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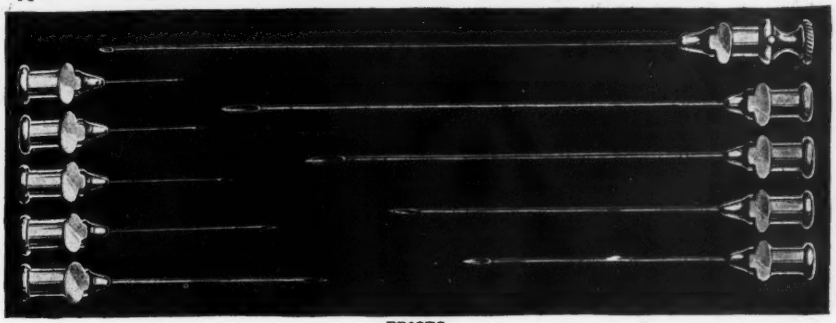

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⅝" and ¾"	23 "	4.50 " "	1½"	20 Guage	1.00 each	3 "	17 "	4.00 "
1"	21 "	6.00 " "	2"	19 "	2.00 "	3½"	17 "	5.00 "

To the Practitioner who is unable to secure these Needles otherwise, we will mail postpaid one dozen assorted needles from ⅜" to 1¼" upon receipt of five dollars.

When ordering, it is important to mention the kind of syringe the needles are required to fit.

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50% BETTER

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1. All claims or suits for alleged civil malpractice, error or mistake, for which our contract holder,
2. Or his estate is sued, whether the act or omission was his own,
3. Or that of any other person (not necessarily an assistant or agent),
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6. Defense through the court of last resort and until all legal remedies are exhausted.
7. Without limit as to amount expended.
8. You have a voice in the selection of local counsel.
9. If we lose, we pay to amount specified in addition to the unlimited defense.
10. The only contract containing all the above features and which is protection per se.

A sample upon request

THE MEDICAL PROTECTIVE CO.
of FT. WAYNE, IND.
Professional Protection Exclusively

SAVE TWO-THIRDS

Sherman's Bacterial Vaccines

when administered early, will reduce the average course of acute infections like

Pneumonia, Broncho-Pneumonia, Sepsis, Erysipelas, Mastoiditis, Rheumatic Fever, Cold, Bronchitis, etc.

to less than one-third their usual mortality and duration.

Sherman's Bacterial Vaccines are prepared in our specially constructed Laboratories, devoted exclusively to the manufacture of these preparations and are marketed in standardized suspensions.

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Low Alveolar CO_2 Tension
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High Hydrogen-ion Acidity of Blood
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